REVIEW

Acute non-cirrhotic portal vein thrombosis : review

A. Salembier[1], M. Verhamme[2], P. Verhamme[3], W. Van Moerkercke[2,4]

(1) Resident Internal Medicine, UZ Leuven, Herestraat 49, 3000 Leuven, Belgium ; (2) Gastro-enterology, AZ Groeninge, Kennedylaan 4, 8500 Kortrijk, Belgium ; (3) Cardiology, Vascular Medicine, UZ Leuven, Herestraat 49, 3000 Leuven, Belgium ; (4) Gastro-enterology, UZ Leuven, Herestraat 49, 3000 Leuven, Belgium.

Abstract

A 35-year-old men with a medical history of myocardial infarction, presenting with fever, general malaise and vague abdominal discomfort, was diagnosed with a portomesenteric venous thrombosis and acute cytomegalovirus (CMV) infection. Thrombophilia screening resulted in detection of heterozygosity for factor II G20210A gene mutation. Low molecular weight heparin in therapeutic dose was started, followed by disappearance of thrombus on imaging CT two months after diagnosis. The multifactorial origin of portal thrombosis and the importance of awareness of the link between CMV infection and an increased risk of thrombosis is emphasized with this case and review of the literature. Identifying CMV infection as a trigger for thrombosis can help to avoid extended anticoagulation.

Acute non-cirrhotic PVT is a rare but probably underestimated condition as symptoms may be discrete or non-specific. The origin of portal thrombosis is frequently multifactorial. Recent literature has emphasized the increasing prevalence of CMV-induced PVT in immunocompetent patients. The multifactorial origin of portal thrombosis and the importance of awareness of the link between CMV infection and an increased risk of thrombosis is emphasized with this review of the literature and included case. Identifying CMV infection as a trigger for thrombosis can help to avoid extended anticoagulation. (Acta gastroenterol. belg., **2018**, 81, **318-322**).

Keywords : Cytomegalovirus, factor II G20210 mutation, portomesenteric vein thrombosis.

Case report

A 35-year-old men presented to the gastro-enterology out-patient clinic of a secondary centre Belgian hospital with complaints of general malaise and fever for 2 weeks. Furthermore he had a difficult to describe abdominal discomfort, but declined to having pain. Appetite had lessened and he reported having lost 3 to 4 kg of weight in the last 2 weeks.

Medical history was remarkable for an ST-elevation myocardial infarction at the age of 31 secondary to a thrombotic subocclusion of the proximal LAD coronary artery. Thrombus aspiration was performed, resulting in good patency of the affected vessel. Furthermore he had an appendectomy at younger age. Medications were aspirin 80mg daily, nebivolol 5mg daily and simvastatin 40mg daily. He had no known allergies. The patient had a history of smoking, but had quit at the time of his myocardial infarction. However, his alcohol intake was still substantial (around 20 units a week). Family history revealed that his father too had suffered from an acute myocardial infarction at the age of 40. However, it had remained unclear if this was due to thrombosis or a stenotic lesion.

On physical examination, the patient appeared ill but he was not in distress. He had a temperature of 38°C, a regular pulse of 93 beats per minute and a blood pressure of 101/39 mmHg. Oxygen saturation was 99%. Cardiac examination was normal, with no murmurs, rubs or jugular venous distension. Both lungs were clear at auscultation. The abdomen was nontender and without palpable organomegaly. No jaundice was noticed, nor were there any rashes. Neurologic examination was normal. A presumptive diagnosis of viral illness was made and the patient was admitted to the hospital for further evaluation.

Ultrasound examination of the abdomen revealed slight hepatomegaly with steatosis and splenomegaly with bipolar diameter of 13 to 14 cm. A surprising finding of a hyperechogenic reflection located in the splenic vein near the venous confluence was made, compatible with venous thrombosis (Fig 1). Computed tomography scanning of the abdomen revealed a thrombosis of the superior mesenteric vein and the splenic vein progressing into the portal vein (Fig 2). Also slight pleural and pericardial effusions were noted.

Biochemical blood analysis revealed minor inflammation with a CRP level of 18.4 mg/l (ref. 0.00-5.0)

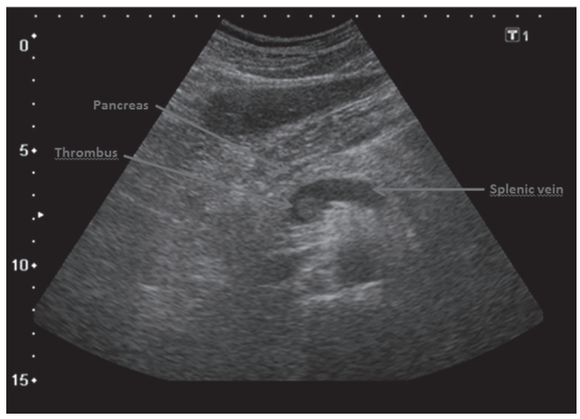

Fig 1. — Ultrasound still showing a hyperechogenic reflection located in the splenic vein near the venous confluence

Correspondence to : A. Salembier, Resident Internal Medicine, UZ Leuven, Herestraat 49, 3000 Leuven,
Email: alexander.salembier@uzleuven.be

Submission date : 22/10/2016
Acceptance date : 05/01/2018

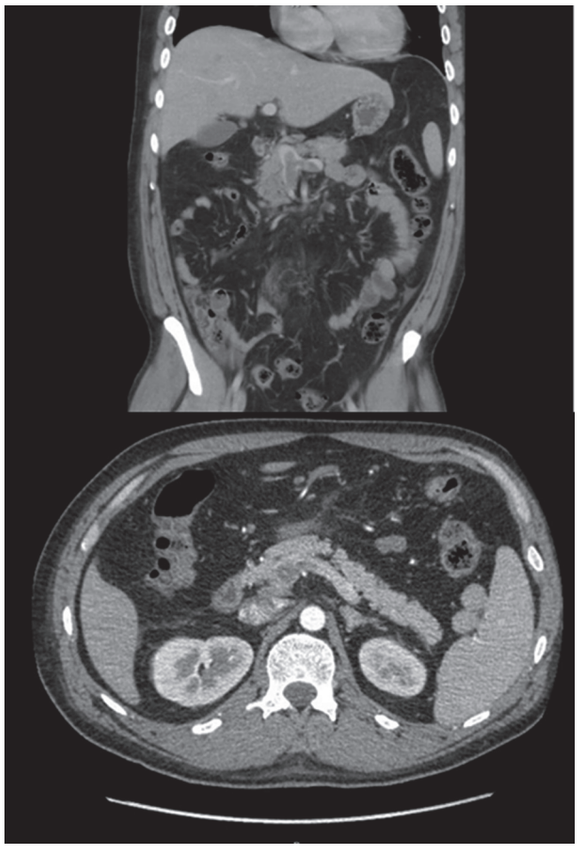

Fig 2. — Transverse and coronal CT image of the abdomen showing thrombosis of the superior mesenteric vein and the splenic vein progressing into the portal vein.

with an absolute lymphocytosis of 7500 per cubic millimeter (ref. 1300-4000). The patient was slightly anaemic with a haemoglobin level of 12.4 g/dl (ref. 13.5-17.5). Platelet count was normal. Creatinine level was 0.85 mg/dl (ref. 0.59-1.20), urea 14.6 mg/dl (ref. 15.0-49.0). The serum level of aspartate aminotransferase was 62 U/l (ref. 0-37), alanine aminotransferase 57 U/l (ref. 0-43), gamma-glutamyl transferase 69 U/l (ref. <60). Bilirubin level and alkaline phosphatase level were normal. Thyroid function was normal, as were measurements of corticotropic function. Urinalysis revealed little proteinuria (0.180 g/g creatinine (ref. <0.150)) and leucocyturia (16 per cubic millimetre (ref. 0-10)). Blood cultures were negative. Viral serology revealed strongly positive cytomegalovirus (CMV) IgM antibodies titre and weakly positive CMV IgG titre (12.8 IU/ml (ref. <1)).

We diagnosed an acute portomesenteric venous thrombosis, provoked by an acute CMV-infection. Low molecular weight heparin (LMWH) in therapeutic dose was started. In view of earlier coronary thrombosis, thrombophilia testing was performed. This patient appeared to be heterozygous for factor II G20210A gene mutation. Imaging of thorax and abdomen did not reveal any malignancies. Abdominal CT performed two months after diagnosis showed a normal patency of the superior mesenteric vein, splenic vein and portal vein. The patient was kept on LMWH for 2 months, after which he was switched to vitamin K antagonists.

We concluded that the portomesenteric venous thrombosis had been triggered by a CMV-induced hypercoagulability in a patient with an inherently higher risk for thrombosis due to factor II G20210A gene mutation heterozygosity.

Introduction

Splanchnic vein thrombosis, including mesenteric, splenic and portal vein thrombosis (PVT), is a rare condition with an estimated incidence of 4 per million patients (1). However, this may be an underestimation as an autopsy study showed a prevalence of around 1% (2). PVT may be clinically silent or present with abdominal pain, fever and other non-specific dyspeptic symptoms (3).

The following case of a 35-year-old man presenting to the gastro-enterology out-patient clinic illustrates the vague symptomatology of patients with PVT. The patient presented with complaints of general malaise and fever for 2 weeks, furthermore he had a difficult to describe abdominal discomfort, but declined to having pain. Appetite had lessened and he reported having lost 3 to 4 kg of weight in the last 2 weeks.

Medical history was remarkable for an ST-elevation myocardial infarction at the age of 31 caused by a thrombotic subocclusion of the proximal LAD coronary artery. The patient had a history of smoking, but had quit at the time of his myocardial infarction. However, his alcohol intake was still substantial (around 20 units a week). Family history revealed that his father also had an acute myocardial infarction at the age of 40. However, it had remained unclear if this was due to thrombosis or a stenotic lesion.

On physical examination, the patient appeared ill but he was not in distress. He had a temperature of 38°C, a regular pulse of 93 beats per minute and a blood pressure of 101/39 mmHg. Oxygen saturation was 99%. The abdomen was nontender and without palpable organomegaly. No jaundice was noticed. Ultrasound examination of the abdomen revealed slight hepatomegaly with steatosis and splenomegaly with bipolar diameter of 13 to 14 cm. A surprising finding of a hyperechogenic reflection located in the splenic vein near the venous confluence was made, compatible with venous thrombosis (Fig 1). Computed tomography scanning of the abdomen revealed a thrombosis of the superior mesenteric vein and the splenic vein progressing into the portal vein (Fig 2). Biochemical blood analysis revealed minor inflammation with a CRP level of 18.4 mg/l (ref. 0.00-5.0) with an absolute lymphocytosis of 7500 per cubic millimeter (ref. 1300-4000). Viral serology revealed strongly positive cytomegalovirus (CMV) IgM antibody titre and weakly positive CMV IgG

titre (12.8 IU/ml (ref. <1)). In view of earlier coronary thrombosis, thrombophilia testing was performed. This patient appeared to be heterozygous for factor II G20210A gene mutation.

We concluded that the portomesenteric venous thrombosis had been triggered by a CMV-induced hypercoagulability in a patient with an inherently higher risk for thrombosis due to factor II G20210A gene mutation heterozygosity.

Three main variants of PVT can be distinguished: acute non-cirrhotic PVT, acute cirrhotic PVT and chronic PVT (4). This review will only focus on acute non-cirrhotic PVT.

Risk factors for portal thrombosis

The pathophysiology of acute non-cirrhotic PVT is based on the features of Virchow's triad, i.e. a hypercoagulable state, vascular endothelial injury or reduced portal flow (table 1) (4). Risk factors for a **hypercoagulable state** are generally divided into congenital and acquired risks (5). Congenital factors encompass antithrombin deficiency, protein C deficiency, protein S deficiency, factor V Leiden mutation and factor II G20210A mutation. Acquired risk factors include malignancy, chronic inflammatory diseases, hormonal therapy, pregnancy, myeloproliferative disorders (JAK2-mutation), paroxysmal nocturnal hemoglobinuria, hyperhomocysteinemia and antiphospholipid syndrome (4). Recently, mutations in thrombin activatable fibrinolysis inhibitor (TAFI) gene and increased factor VIII levels have been shown to be associated with development of PVT (4,5). A link with cytomegalovirus infection has also been demonstrated in the last decade (6). PVT may be secondary to **vascular endothelial injury** due to local risk factors such as intra-abdominal inflammatory diseases (e.g. pancreatitis, cholecystitis, cholangitis, appendicitis,…), surgery (e.g. splenectomy, colectomy, portacaval shunts) and abdominal trauma. Compression or direct vascular invasion by hepatocellular carcinoma and cholangiocarcinoma may lead to **reduced portal blood flow** and consequently thrombosis. Compression may also occur with enlargement of lymph nodes in tuberculosis or lymphoma (4).

Presentation and diagnosis of acute portal vein thrombosis

Acute non-cirrhotic PVT usually presents with abdominal pain (91%), fever (35%), ascites (38%) and splenomegaly (37%). Thrombosis of the superior mesenteric vein may lead to intestinal ischemia with subsequent bowel infarction and ileus, which can then present with haematochezia, rebound tenderness, fever and ascites. Partial thrombotic obstruction may be associated with fewer symptoms (4).

Liver function is generally normal in acute non-cirrhotic PVT. D-dimers are usually increased, coagulation factors may be disturbed (4). Although ultrasound is the cornerstone in the workup as it is quickly accessible and less expensive, there is an interpatient variability and operator dependency. PVT is shown as solid isoechoic material within the veins (1). Sensitivity and specificity range from 80 to 100% (4). CT and MRI are more suited to provide information about extension of thrombosis, bowel infarction and presence of an underlying malignancy. PVT is shown as isodense or hyperdense intravenous material on non-contrast-enhanced CT and as hypodense and non-enhancing on contrast-enhanced CT. Tumour thrombus will enhance (4). MRI has a sensitivity and specificity of 100% and 98% respectively for detecting PVT. MR portography is superior to colour Doppler ultrasound in detecting PVT (4). Splenoportovenography has become obsolete with the introduction of described non-invasive imaging (4). Gastroscopy is useful in patients with cirrhosis, malignancy or more chronic PVT to exclude hypertensive gastropathy and oesophageal varices (4). After diagnosis of a non-cirrhotic PVT an extensive procoagulant work-up can help to identify predisposing factors (4).

Inherited thrombophilia and the risk of portal vein thrombosis

A large cohort study (En-Vie study) with 105 patients with non-malignant, non-cirrhotic PVT reported inherited prothrombotic factors in 35% (7-9). The exact prevalence of each inherited deficiency is difficult to determine due to confounding factors; reduced liver synthesis function and acute thrombosis itself might cause lower levels of antithrombin, protein C and protein S, vitamin K antagonists may interfere with the diagnosis of protein C and S deficiency and assays for lupus anticoagulant might be falsely positive when using vitamin K antagonists (5,10). Recent studies suggest a prevalence of antithrombin deficiency in PVT between 0-5%, of protein C deficiency between 0-7% and of protein S deficiency between 0-30% (5). The prevalence of factor V Leiden mutation in PVT is estimated at 3-9% (11). The prevalence of prothrombin G20210A mutation was 14% in the En-Vie study (7). Prothrombin gene mutation is associated with PVT but not with Budd-Chiari syndrome, unlike factor V Leiden mutation (12). Antiphospholipid antibodies are considered a risk factor for PVT. Prevalence is estimated at 5-15%, but case-control studies have been lacking (5). Elevated factors VIII levels have been found in patients with PVT without cirrhosis, a finding recently confirmed in a Chinese population (13,14). Heterozygotes or non-carriers of the 147Thr allele of the TAFI gene have a significantly increased risk of PVT, carriers of the 325Ile allele have a slightly increased risk of PVT, though not significantly (15). JAK2-V617F mutation is also a risk factor for splanchnic vein thrombosis (8).

CMV-induced thrombogenicity in portal vein thrombosis

Previously thought to be a rare complication of CMV infection, recent case reports and case series have emphasized the increasing prevalence of CMV-induced (portal) thrombosis in immunocompetent patients (3,6,16,17,18,19,20). According to a case-control study of Atzmony et al. the incidence of (venous and arterial) thrombosis following acute CMV infection could be as high as 6.4%, which was significantly higher than in the non-infected cohort (p=0.004) (21). A more recent Dutch case-control study found a trend of more frequent active CMV-infection in patients with venous thrombosis (22). A review of Justo et al. in 2011 cited 64 cases of CMV-associated thrombosis in immunocompetent patients, 24 of which had splanchnic thrombosis (23). The majority of patients had other prothrombotic predispositions, most frequently oral contraception, antiphospholipid syndrome or Factor V Leiden, confirming the frequent multifactorial aetiology predisposing for thrombosis (23). In a Belgian cohort 90% of patients with venous thromboembolism associated with acute cytomegalovirus infection had an underlying hereditary thrombophilia (24).

As to the mechanism of CMV-induced thrombosis, several theories are proposed: a CMV-induced production of antiphospholipid antibodies, enhanced adhesion of platelets and leucocytes onto CMV-infected endothelial cells with subsequent local inflammatory response and tissue-factor exposure and intrinsic CMV procoagulant properties which are probably acquired after envelope constitution from the modified endothelial membrane with consequent enhanced production of coagulation factors (25,26,27).

Treatment of portal vein thrombosis

After the diagnosis of PVT, a work-up is initiated to exclude cirrhosis, an inflammatory abdominal focus and malignancy. Concurrent, often multiple, risk factors for thrombosis should be thoroughly investigated (Table 1) (28). In general, patients with non-cirrhotic, non-malignant acute PVT are treated with anticoagulation therapy and low molecular weight heparin (LWMH) is initiated in most patients. Anticoagulation is continued with LMWH or vitamin K antagonists (8). Long-term therapy is mostly given for three to six months, but depending on underlying causes and risk factors duration of therapy can be shortened or extended, sometimes indefinitely (28,29). Rarely local or systemic thrombolysis is used (29,30,31). This might be indicated in patients with thrombus extension or worsening pain while on therapeutic anticoagulation and in patients with bowel necrosis due to thrombosis (32). A randomized controlled trial of anticoagulation for acute PVT is not realistic due to the rarity and heterogeneity of the disorder (7). New oral anticoagulants have not been studied in this patient population (32). Spontaneous recanalization after PVT may occur (7,29).

Table 1. — **Risk factors for portal vein thrombosis**

Hypercoagulable state
- Congenital risk factors:
° Antithrombin deficiency
° Protein C deficiency
° Protein S deficiency
° Factor V Leiden
° Factor II G20210 mutation
° Dysfibrinogenemia
° Non-O blood group
- Acquired risk factors:
° Malignancy
° Chronic inflammatory disease
° Hormonal therapy
° Pregnancy
° Myeloproliferative disorders (JAK2-mutation)
° Paroxysmal nocturnal hemoglobinuria
° Hyperhomocystinemia
° Antiphospholipid syndrome
° Thrombin activatable fibrinolysis inhibitor gene mutation
° Increased factor VIII
° CMV infection o HIT
° Behçet
Vascular endothelial injury
° Intra-abdominal inflammatory diseases
▪ Appendicitis, cholecystitis, cholangitis, pancreatitis, diverticulitis, abdominal abscess
° Abdominal surgery o Abdominal trauma
Reduced portal flow
° Compression of invasion by tumor
° Enlarged lymph nodes (tuberculosis, lymphoma)

Few studies have focused on the risk of recurrence of PVT (5). Condat et al. showed a recurrence rate of thrombosis of 5.5 per 100 person-years, with an underlying prothrombotic state as an independent risk factor for recurrence (5). A recent study by Spaander et al. showed a recurrence of PVT in 4%, 8% and 27% of patients after 1, 5 and 10 years, respectively. There was a trend towards lower recurrence rate with anticoagulant therapy (P=0.1). The only significant predictor of recurrent thrombotic events was the presence of an underlying prothrombotic disorder (P=0.03) (33). The bleeding risk at 1, 5 and 10 years was 19%, 46% and 49%, respectively, with mainly variceal bleeding events. Anticoagulation therapy was a significant predictor of bleeding (P=0.01) (33). In this regard, it is difficult to give recommendations on the duration of anticoagulant therapy. Long term therapy should probably be reserved to those patients with a major thrombophilic risk factor or recurrent thrombosis (5).

The mainstay of therapy in patients with acute PVT and concurrent CMV infection is also anticoagulation, either low molecular weight heparin or warfarin. Thrombolysis has been used in CMV-induced acute PVT (34). The duration of therapy in literature ranges from 20 days to 9 months (23). The decision whether to stop anticoagulation was based on resolution of thrombosis on imaging or a decrease in antiphospholipid antibody levels (3). Theoretically, long term therapy should not be necessary, provided no other underlying thrombophilic risk factors are found. Although anecdotally used, we could find no data on the benefit of treatment with

ganciclovir in immunocompetent patients (20). In view of previous thrombosis and underlying heterozygosity for factor II G20210A gene mutation, our patient was treated with LMWH for 2 months, after which he was switched to vitamin K antagonist indefinitely.

Conclusion

Acute PVT is a rare but probably underestimated condition as symptoms may be discrete or non-specific. The origin of portal thrombosis is frequently multifactorial. Recent literature has emphasized the increasing prevalence of CMV-induced PVT in immunocompetent patients. Identifying CMV infection as a trigger for thrombosis can help to avoid extended anticoagulation.

References

1. SABOL TP, MOLINA M, WU GY. Thrombotic Venous Diseases of the Liver. *Journal of Clinical and Translational Hepatology*, 2015, **3** : 189-94.
2. OGREN M, BERGQVIST D, BJÖRCK M, ACOSTA S, ERIKSSON H, STERNBY NH. Portal vein thrombosis: prevalence, patient characteristics and lifetime risk: a population study based on 23,796 consecutive autopsies. *World J. Gastroenterol*., 2006, **12** : 2115-2119.
3. WANG T, KUTTIKAT A, PULSALKAR P, NANGUZGAMBO A, BHALARA S. Cytomegalovirus-associated portal vein thrombosis in an immunocompetent patient: an underestimated complication. Oxford Medical *Case Reports*, 2015, **5** : 294–296.
4. CHAWLA YK, BODH V. Portal vein thrombosis. Journal of Clinical and Experimental Hepatology. 2015;5(1):22–40.
5. LEEBEEK F, SMALBERG J, JANSSEN H. Prothrombotic disorders in abdominal vein thrombosis. *Netherlands Journal of Medicine*, 2012, **70** : 400-405.
6. SQUIZZATO A, AGENO W, CATTANEO A, BRUMANA N. A case report and literature review of portal vein thrombosis associated with cytomegalovirus infection in immunocompetent patients. *Clinical infectious diseases*, 2007, **44** : e13-6.
7. PLESSIER A, DARWISH-MURAD S, HERNANDEZ-GUERRA M, CONSIGNY Y, FABRIS F, TREBICKA J, *et al.* Acute portal vein thrombosis unrelated to cirrhosis: a prospective multicenter follow-up study. *Hepatology*, 2010, **51** : 210-8.
8. AGENO W, RIVA N, SCHULMAN S, BEYER-WESTENDORF J, BANG SM, SENZOLO M, *et al*. Long-term clinical outcomes of splanchnic vein thrombosis: results of an international registry. *JAMA Intern. Med*., 2015, **175** : 1474-80.
9. RIVA N, AGENO W, SCHULMAN S, BEYER-WESTENDORF J, DUCE R, MALATO A, *et al.* Clinical history and antithrombotic treatment of incidentally detected splanchnic vein thrombosis: a multicenter international prospective registry. *Lancet Haematol.*, 2016, **3** : 267-75.
10. ISERT M, MIESBACH W, STOEVER G, LINGHOFF-LAST E, LINNEMAN B. Screening for lupus anticoagulants in patients treated with vitamin K antagonists. *Int. J. Lab. Hematol*., 2015, **37** : 358-65.
11. SMALBERG JH, KRUIP MJ, JANSSEN HL, RIJKEN DC, LEEBEEK FW, DE MAAT MP. Hypercoagulability and hypofibrinolysis and risk of deep vein thrombosis and splanchnic vein thrombosis: similarities and differences. *Arterioscler Thromb. Vasc. Biol.*, 2011, **31** : 485-93.
12. QI X, REN W, DE STEFANO V, FAN D. Associations of coagulation factor V Leiden and Prothrombin G20210A mutations with Budd-Chiari syndrome and portal vein thrombosis: a systematic review and meta-analysis. *Clinical gastroenterology and hepatology*, 2014, **12** : 1801-12.
13. MARTINELLI I, PRIMIGNANI M, AGHEMO A, REATI R, BUCCIARELLI P, BATTAGLIOLI T, et al. High levels of factor VIII and risk of extra-hepatic portal vein obstruction. *J. Hepatol*., 2009, **50** : 916-22.
14. CHEN H, LIU L, QI X, HE C, YIN Z, WU F, *et al*. Imbalance of pro- vs. anti-coagulation factors in Chinese patients with Budd-Chiari syndrome and non-cirrhotic portal vein thrombosis. *PLoS One*, 201, **30** : e0119909.
15. DE BRUIJNE EL, DARWISH MURAD S, DE MAAT MP, TANCK MW, HAAGSMA EB, VAN HOEK B, *et al.* Genetic variation in thrombin-activatable fibrinolysis inhibitor (TAFI) is associated with the risk of splanchnic vein thrombosis. *Thromb. Haemost*., 2007, **97** : 181-5.
16. GALLOULA A, ROSSI A, GAUTIER V, MINOZZI C, MESSAS E, MIRAULT T. Thrombose portale associée à une infection aiguë à cytomegalovirus. *Journal des maladies vasculaires*, 2014, **39** : 224-30.
17. KRÄHENMANN P, DÜRIG R, SENDI P, OESTMANN A. Persistent fever in the elderly. *Praxis*, 2011, **100** : 985-8.
18. SCHREINER M, BARCK T, FOROUTAN B, BAUMGARTEN U. A rare caus of portal vein thrombosis in a previously healthy young man with acute hepatitis. *J. Clin. Virol*., 2011, **51** : 152-4.
19. MASSOURE MP, EZANNO AC, MILLOT I, FIXOT K, REY P, SOCKEEL P. Acute portal vein thrombosis associated with acute cytomegalovirus infection in an immunocompetent adult and complicated with an abdominal compartment syndrome. Gastroenterol. *Clin. Biol*., 2010, **34** : e3-5.
20. LADD AM, GOYAL R, ROSAINZ L, BAIOCCO P, DIFABRIZIO L. Pulmonary embolism and portal vein thrombosis in an immunocompetent adolescent with acute cytomegalovirus hepatitis. *J. Thromb. Thrombolysis*, 2009, **28** : 496-9.
21. ATZMONY L, HALUTZ O, AVIDOR B, FINN T, ZIMMERMAN O, STEINVIL A, *et al*. Incidence of cytomegalovirus-associated thrombosis and its risk factors : a case-control study. *Thromb. Res*., 2010, **126** : e439-43.
22. TICHELAAR VY, SPRENGER HG, MÄKELBURG AB, NIESTERS BG, KLEIN-NELEMANS HC, LIJFERING WM. Active cytomegalovirus infection in patients with acute venous thrombosis : a case-control study. *Am. J. Hematol.*, 2011, **86** : 510-2.
23. JUSTO D, FINN T, ATZMONY L, GUY N, STEINVIL A. Thrombosis associated with acute cytomegalovirus infection : a meta-analysis. *Eur. J. Intern. Med*., 2011, **22** : 195-9.
24. YILDIZ H, ZECH F, HAINAUT P. Venous thromboembolism associated with acute cytomegalovirus infection : epidemiology and predisposing conditions. *Acta Clin. Belg*., 2016, **71** : 231-4.
25. TSUYOSHI N, MITSUTERU A, KENSUKE I, YASUTAKA K, YOJIRO A, HIROAKE N, *et al.* Transient antiphospholipid syndrome associated with primary cytomegalovirus infection : A case report and literature review. Case Rep. Rheumatol., 2014, 271548.
26. LUCA GALLI, GERDES VEA, GUASTI L, SQUIZZATO A. Thrombosis associated with viral hepatitis. *J. Clin. Transl. Hepatol*., 2014, **2** : 234-239.
27. SQUIZZATO A, GERDES VEA, BÜLLER HR. Effects of human cytomegalovirus infection on the coagulation system. *Thromb. Haemost*., 2005, **93** : 403-410.
28. DELEVE LD, VALLA D-C, GARCIA-TSAO G. Vascular disorders of the liver. *Hepatology*, 2009, **49**(5) : 1729-64.
29. HALL TC, GARCEA G, METCALFE M, BILKU D, DENNISON AR. Management of acute non-cirrhotic and non-malignant portal vein thrombosis: A systematic review. *World Journal of Surgery,* 2011, **35** : 2510-20.
30. JUNG HJ, LEE SS. Combination of surgical thrombectomy and direct thrombolysis in acute abdomen with portal and superior mesenteric vein thrombosis. *Vascular Specialist International*, 2014, **30** : 155-8.
31. BROWN L, ABBASS AA, NAGAI S, PATIL V, ABOULJOUD M, GETZEN T, *et al.* Thrombolysis of portal vein thrombosis after splenectomy following liver transplantation. *Liver Transpl.*, 2013, **19** : 346-8.
32. SHARMA AM, ZHU D, HENRY Z. Portal vein thrombosis : when to treat and how? *Vascular medicine*, 2016, **21** : 61-69.
33. SPAANDER MC, HOEKSTRA J, HANSEN BE, VAN BUUREN HR, LEEBEEK FW, JANSSEN HL. Anticoagulant therapy in patients with non-cirrhotic portal vein thrombosis: effect on new thrombotic events and gastrointestinal bleeding. *Journal of thrombosis and haemostasis*, 2013, **11** : 452-9.
34. VAN MOERKERCKE W, PAUWELYN K, BRUGMAN E, VERHAMME M. Cytomegalovirus-associated superior mesenteric vein thrombosis treated with systemic and in situ-thrombolysis. *Eur. J. Gastroenterol. Hepatol*., 2009, **21** : 587-92.