# World Journal of *Clinical Cases*

World J Clin Cases 2022 April 26; 10(12): 3639-3968





Published by Baishideng Publishing Group Inc

W J C C World Journal of Clinical Cases

#### Contents

#### Thrice Monthly Volume 10 Number 12 April 26, 2022

#### **EVIDENCE REVIEW**

3639 Tilt and decentration with various intraocular lenses: A narrative review Chen XY, Wang YC, Zhao TY, Wang ZZ, Wang W

#### **REVIEW**

3647 Role of zonula occludens in gastrointestinal and liver cancers Ram AK, Vairappan B

#### **MINIREVIEWS**

3662 Pathophysiological mechanisms of hepatic stellate cells activation in liver fibrosis Garbuzenko DV

#### **ORIGINAL ARTICLE**

#### **Retrospective Cohort Study**

3677 Predictors of unfavorable outcome at 90 days in basilar artery occlusion patients Chiu YC, Yang JL, Wang WC, Huang HY, Chen WL, Yen PS, Tseng YL, Chen HH, Tsai ST

#### **Retrospective Study**

- 3686 Role of multidetector computed tomography in patients with acute infectious colitis Yu SJ, Heo JH, Choi EJ, Kim JH, Lee HS, Kim SY, Lim JH
- Efficacy and prognostic factors of neoadjuvant chemotherapy for triple-negative breast cancer 3698 Ding F, Chen RY, Hou J, Guo J, Dong TY
- 3709 Relationship between subgroups of central and lateral lymph node metastasis in clinically node-negative papillary thyroid carcinoma Zhou J, Li DX, Gao H, Su XL
- Nomogram to predict postoperative complications in elderly with total hip replacement 3720 Tan XJ, Gu XX, Ge FM, Li ZY, Zhang LQ
- 3729 Flap failure prediction in microvascular tissue reconstruction using machine learning algorithms Shi YC, Li J, Li SJ, Li ZP, Zhang HJ, Wu ZY, Wu ZY

#### **Observational Study**

Surgery in platinum-resistant recurrent epithelial ovarian carcinoma 3739 Zhao LQ, Gao W, Zhang P, Zhang YL, Fang CY, Shou HF



World Journal of Clinical Cases

#### Thrice Monthly Volume 10 Number 12 April 26, 2022

3754 Anorectal dysfunction in patients with mid-low rectal cancer after surgery: A pilot study with threedimensional high-resolution manometry

Pi YN, Xiao Y, Wang ZF, Lin GL, Qiu HZ, Fang XC

#### **Randomized Controlled Trial**

3764 Effect of wrist-ankle acupuncture on propofol dosage during painless colonoscopy: A randomized controlled prospective study

He T, Liu C, Lu ZX, Kong LL, Li Y, Xu Z, Dong YJ, Hao W

#### **META-ANALYSIS**

Contents

- 3773 Melatonin intervention to prevent delirium in hospitalized patients: A meta-analysis You W, Fan XY, Lei C, Nie CC, Chen Y, Wang XL
- 3787 Risk factors for hospital readmissions in pneumonia patients: A systematic review and meta-analysis Fang YY, Ni JC, Wang Y, Yu JH, Fu LL

#### **CASE REPORT**

3801 Anti-programmed death 1 antibody in the treatment of coexistent Mycobacterium fortuitum and lung cancer: A case report

Zhang CC, Chen P

- 3808 Acute pancreatitis-induced thrombotic thrombocytopenic purpura: A case report Wang CH, Jin HF, Liu WG, Guo Y, Liu Z
- 3814 Successful management of life-threatening aortoesophageal fistula: A case report and review of the literature

Zhong XQ, Li GX

3822 Isolated coagulopathy without classic CRAB symptoms as the initial manifestation of multiple myeloma: A case report

Zhang Y, Xu F, Wen JJ, Shi L, Zhou QL

3828 Evaluation of intracoronary function after reduction of ventricular rate by esmolol in severe stenotic myocardial bridge: A case report

Sun LJ, Yan DG, Huang SW

3834 Pediatric living donor liver transplantation using liver allograft after ex vivo backtable resection of hemangioma: A case report

Li SX, Tang HN, Lv GY, Chen X

- 3842 Kimura's disease in soft palate with clinical and histopathological presentation: A case report Li W
- 3849 Combined targeted therapy and immunotherapy in anaplastic thyroid carcinoma with distant metastasis: A case report

Ma DX, Ding XP, Zhang C, Shi P



•	World Journal of Clinical Cases							
Conten	Thrice Monthly Volume 10 Number 12 April 26, 2022							
3856	Successful multimodality treatment of metastatic gallbladder cancer: A case report and review of literature							
	Zhang B, Li S, Liu ZY, Peiris KGK, Song LF, Liu MC, Luo P, Shang D, Bi W							
3866	Ischemic colitis after receiving the second dose of a COVID-19 inactivated vaccine: A case report							
	Cui MH, Hou XL, Liu JY							
3872	Cryoballoon pulmonary vein isolation and left atrial appendage occlusion prior to atrial septal defect closure: A case report							
	Wu YC, Wang MX, Chen GC, Ruan ZB, Zhang QQ							
3879	Surgical treatment for a combined anterior cruciate ligament and posterior cruciate ligament avulsion fracture: A case report							
	Yoshida K, Hakozaki M, Kobayashi H, Kimura M, Konno S							
3886	Successful robot-assisted partial nephrectomy for giant renal hilum angiomyolipoma through the retroperitoneal approach: A case report							
	Luo SH, Zeng QS, Chen JX, Huang B, Wang ZR, Li WJ, Yang Y, Chen LW							
3893	Cryptococcal antigen testing of lung tissue homogenate improves pulmonary cryptococcosis diagnosis: Two case reports							
	Wang WY, Zheng YL, Jiang LB							
3899	Combined use of extracorporeal membrane oxygenation with interventional surgery for acute pancreatitis with pulmonary embolism: A case report							
	Yan LL, Jin XX, Yan XD, Peng JB, Li ZY, He BL							
3907	Dynamic navigation system-guided trans-inferior alveolar nerve implant placement in the atrophic posterior mandible: A case report							
	Chen LW, Zhao XE, Yan Q, Xia HB, Sun Q							
3916	Anti-glomerular basement membrane disease with IgA nephropathy: A case report							
	Guo C, Ye M, Li S, Zhu TT, Rao XR							
3923	Amniotic membrane transplantation in a patient with impending perforated corneal ulcer caused by <i>Streptococcus mitis</i> : A case report and review of literature							
	Hsiao FC, Meir YJJ, Yeh LK, Tan HY, Hsiao CH, Ma DHK, Wu WC, Chen HC							
3930	Steriod for Autoimmune pancreatitis complicating by gastric varices: A case report							
	Hao NB, Li X, Hu WW, Zhang D, Xie J, Wang XL, Li CZ							
3936	Antithrombotic treatment strategy for patients with coronary artery ectasia and acute myocardial infarction: A case report							
	Liu RF, Gao XY, Liang SW, Zhao HQ							
3944	Mesh plug erosion into the small intestine after inguinal hernia repair: A case report							
	Xie TH, Wang Q, Ha SN, Cheng SJ, Niu Z, Ren XX, Sun Q, Jin XS							
3951	Recurrence of infectious mononucleosis in adults after remission for 3 years: A case report							
	Zhang XY, Teng QB							



Conter	World Journal of Clinical Cases Thrice Monthly Volume 10 Number 12 April 26, 2022
3959	Vertical direction impaction of kissing molars: A case report Wen C, Jiang R, Zhang ZQ, Lei B, Yan YZ, Zhong YQ, Tang L

Comment on "Outcomes of different minimally invasive surgical treatments for vertebral compression 3966 fractures: An observational study"

Ma L, Luo ZW, Sun YY



#### Contents

Thrice Monthly Volume 10 Number 12 April 26, 2022

#### **ABOUT COVER**

Editorial Board Member of World Journal of Clinical Cases, Potluri Leela Ravishankar, MDS, Professor, Department of Periodontics, SRM Kattankulathur Dental College and Hospital, SRM University, Chennai 603203, Tamil Nadu, India. plrs6@yahoo.com

#### **AIMS AND SCOPE**

The primary aim of World Journal of Clinical Cases (WJCC, World J Clin Cases) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

#### **INDEXING/ABSTRACTING**

The WJCC is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2021 Edition of Journal Citation Reports® cites the 2020 impact factor (IF) for WJCC as 1.337; IF without journal self cites: 1.301; 5-year IF: 1.742; Journal Citation Indicator: 0.33; Ranking: 119 among 169 journals in medicine, general and internal; and Quartile category: Q3. The WJCC's CiteScore for 2020 is 0.8 and Scopus CiteScore rank 2020: General Medicine is 493/793.

#### **RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: Ying-Yi Yuan; Production Department Director: Xu Guo; Editorial Office Director: Jin-Lei Wang,

NAME OF JOURNAL World Journal of Clinical Cases	INSTRUCTIONS TO AUTHORS https://www.wjgnet.com/bpg/gerinfo/204
ISSN	GUIDELINES FOR ETHICS DOCUMENTS
ISSN 2307-8960 (online)	https://www.wjgnet.com/bpg/GerInfo/287
LAUNCH DATE	GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
April 16, 2013	https://www.wjgnet.com/bpg/gerinfo/240
FREQUENCY	PUBLICATION ETHICS
Thrice Monthly	https://www.wjgnet.com/bpg/GerInfo/288
EDITORS-IN-CHIEF	PUBLICATION MISCONDUCT
Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku	https://www.wjgnet.com/bpg/gerinfo/208
EDITORIAL BOARD MEMBERS	ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/2307-8960/editorialboard.htm	https://www.wjgnet.com/bpg/gerinfo/242
PUBLICATION DATE	STEPS FOR SUBMITTING MANUSCRIPTS
April 26, 2022	https://www.wjgnet.com/bpg/GerInfo/239
COPYRIGHT	ONLINE SUBMISSION
© 2022 Baishideng Publishing Group Inc	https://www.f6publishing.com

© 2022 Baishideng Publishing Group Inc. All rights reserved. 7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA E-mail: bpgoffice@wjgnet.com https://www.wjgnet.com



W J C C World Journal C Clinical Cases

# World Journal of

Submit a Manuscript: https://www.f6publishing.com

World J Clin Cases 2022 April 26; 10(12): 3822-3827

DOI: 10.12998/wjcc.v10.i12.3822

ISSN 2307-8960 (online)

CASE REPORT

# Isolated coagulopathy without classic CRAB symptoms as the initial manifestation of multiple myeloma: A case report

Ya Zhang, Fang Xu, Jing-Jing Wen, Lin Shi, Qiao-Lin Zhou

Specialty type: Hematology

Provenance and peer review: Unsolicited article; Externally peer

reviewed.

Peer-review model: Single blind

#### Peer-review report's scientific quality classification

Grade A (Excellent): 0 Grade B (Very good): B Grade C (Good): 0 Grade D (Fair): 0 Grade E (Poor): 0

P-Reviewer: Haque N, Bangladesh

Received: July 13, 2021 Peer-review started: July 13, 2021 First decision: November 22, 2021 Revised: December 1, 2021 Accepted: March 4, 2022 Article in press: March 4, 2022 Published online: April 26, 2022



Ya Zhang, Fang Xu, Jing-Jing Wen, Lin Shi, Qiao-Lin Zhou, Department of Hematology, Mianyang Central Hospital, Mianyang 621000, Sichuan Province, China

Corresponding author: Fang Xu, MD, Academic Fellow, Chief Doctor, Department of Hematology, Mianyang Central Hospital, No. 12 Changjia Alley, Jingzhong Street, Fucheng District, Mianyang 621000, Sichuan Province, China. 147377807@qq.com

### Abstract

#### BACKGROUND

Multiple myeloma patients usually present with CRAB symptoms (hypercalcemia, renal disease, anemia and bone diseases) as initial manifestations. Bleeding symptoms are less common, most of which result from thrombocytopenia or infiltration of plasmacytoma. Relatively, coagulopathy is not so common, especially isolated coagulopathy without CRAB manifestations, which is very rare. Herein, we report a 54-year old female who was hospitalized for intermittent and recurrent mild oral mucosal hemorrhage without other bleeding symptoms for almost one month or typical myeloma features.

#### CASE SUMMARY

Two months before admission, the patient underwent implantation of a permanent pacemaker due to sick sinus syndrome. Prothrombin time and activated partial thromboplastin time were significantly prolonged. Factor X deficiency was demonstrated to account for the coagulation dysfunction. An M protein peak was shown by serum protein electrophoresis. 26.11% of abnormal plasma cells were detected in bone marrow by flow cytometry, expressing CD38, CD138, CD56 and intracellular immunoglobulin Kappa light chain. Bone marrow biopsy also proved the presence of abnormal plasma cells, but Congo red stain was negative. The patient was finally diagnosed with multiple myeloma IgA-ĸ type. A literature review indicated that factor X deficiency was highly related to amyloidosis. Before bleeding signs, the patient had cardiac arrhythmia, enlargement of the heart, and progressive heart failure; thus, cardiac amyloidosis was suspected.

#### **CONCLUSION**

Bleeding related to coagulation dysfunction is uncommon in multiple myeloma, especially as the initial manifestation. Amyloidosis is a well-recognized cause of isolated acquired factor X deficiency.

WJCC | https://www.wjgnet.com

Key Words: Multiple myeloma; Coagulation function; Hemorrhage; Factor X; Deficiency; Case report

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core Tip:** Coagulopathy resulting from isolated acquired factorX deficiency is uncommon in myeloma. Typical symptoms in multiple myeloma include hypercalcemia, renal disease, anemia and bone diseases (CRAB). Factor X deficiency could herald the CRAB symptoms, and was reported to be closely related to amyloidosis. Secondary amyloidosis could be reasonably suspected if factor X deficiency is verified in myeloma patient.

Citation: Zhang Y, Xu F, Wen JJ, Shi L, Zhou QL. Isolated coagulopathy without classic CRAB symptoms as the initial manifestation of multiple myeloma: A case report. World J Clin Cases 2022; 10(12): 3822-3827 URL: https://www.wjgnet.com/2307-8960/full/v10/i12/3822.htm DOI: https://dx.doi.org/10.12998/wjcc.v10.i12.3822

#### INTRODUCTION

Multiple myeloma is one of the most common hematological malignancies. Usually myeloma patients initially present with CRAB symptoms (hypercalcemia, renal disease, anemia and bone diseases). As reported, bleeding occurs in almost 7% of *de novo* myeloma patients[1], often combined with CRAB symptoms. Thrombocytopenia and infiltration of plasmacytoma account for most bleeding events. Coagulopathy is not common, especially isolated coagulopathy without CRAB manifestations, which is very rare. Herein, we report a multiple myeloma patient presenting with recurrent bleeding of oral mucosa and coagulopathy as initial manifestations without typical myeloma features.

#### CASE PRESENTATION

#### Chief complaints

A 54-year old female was hospitalized for intermittent and recurrent mild oral mucosal hemorrhage without other bleeding symptoms for almost one month.

#### History of present illness

Initially, the patient presented no weakness, oliguria, edema, bone pain, etc. Drug abuse, and contact with rodenticide and other toxic agents was denied. Coagulation function was assessed two weeks before admission during her first visit to the Hematology Outpatient Department. Prothrombin time (PT) and activated partial thromboplastin time (APTT) were significantly prolonged, and were 20.7 s and 41 s, respectively. Fibrinogen was 1.79 g/L and thrombin time was normal. D dimer and fibrin degradation products were higher than the normal level, and were 6.2 mg/L and 2.29 mg/L, respectively. Considering the prolongation of both PT and APTT, vitamin K1 was administered at 40 to 80 mg/d. Bleeding seemed to initially improve slightly but recurred and became more obvious and frequent. PT and APTT were still longer than normal. The patient also had a cough and expectoration. She was admitted for further investigation and diagnosis.

#### History of past illness

Past history indicated that the patient was a hepatitis B virus carrier. Two months before admission, she underwent implantation of a permanent pacemaker due to sick sinus syndrome in another hospital. Before and after the operation, routine blood tests and laboratory examinations were normal, and PT was 15.7 s. The patient denied taking any other drugs except atorvastatin calcium after discharge.

#### Personal and family history

The patient denied having personal and family history.

#### Physical examination

On admission, several oral blood blisters and spontaneous gingival bleeding were noted. No petechiae, ecchymoses or purpura were observed on the skin. Some wet rales were heard on both sides of the lungs. The heart boundary was enlarged. No splenomegaly, hepatomegaly or masses were found in the abdomen.



#### Laboratory examinations

Laboratory examinations showed that the level of factor II, factor VIII and factor IX were normal, but factor X level was 9.8%. PT delay could be corrected once fresh frozen plasma was used. Routine blood tests revealed normal white blood cell (WBC) count, hemoglobin of 10.7 g/L and platelets of  $90 \times 10^{9}$ /L. Brain natriuretic peptide was 5966 ng/L (normal range < 125 ng/L). Immunoglobulin (Ig)A level was 17.6 g/L, significantly higher than normal (range 1.0-4.2 g/L), while IgG, IgE, and IgM were lower than the normal level.  $\beta$ 2 microglobulin was 4.836 mg/L (normal range 0.9-2.0 mg/L). Blood immunofixation electrophoresis verified the existence of monoclonal immunoglobulin, which was IgA-к type. An M protein peak was shown by serum protein electrophoresis. M protein was 11.26 g/L. Liver function indicated a mild to moderate increase in liver enzymes, including alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl transferase and alkaline phosphatase. Renal function tests showed that creatinine was 67  $\mu$ mol/L, uric acid was 366.5  $\mu$ mol/L, and the glomerular filtration rate was 45.9 mL/min.

#### Imaging examinations

A low dose computed tomography (CT) scan of the whole body did not find any obvious osteolytic lesions. A CT scan and color Doppler ultrasound both indicated enlargement of the heart, especially both atria. Moderate tricuspid regurgitation, mild mitral regurgitation, widened pulmonary artery diameter, mild pulmonary hypertension, a slightly thicker ventricular septum, and mild pericardial effusion were also noted.

#### Further diagnostic work-up

26.11% of plasma cells were detected in bone marrow by flow cytometry, expressing CD38, CD138, CD56 and intracellular immunoglobulin Kappa light chain. The expression of CD38 and CD138 indicated that the abnormal cells were originated from plasma cells. Restricted expression of intracellular immunoglobulin Kappa light chain suggested they were clonal plasma cells. CD56 expression further proved that they were abnormal and neoplastic plasma cells. Bone marrow biopsy also proved the existence of abnormal plasma cells, but Congo red stain was negative.

#### FINAL DIAGNOSIS

Multiple myeloma (IgA-κ type); acquired factor X deficiency; And sick sinus syndrome.

#### TREATMENT

The patient started the first cycle of chemotherapy including bortezomib (1.3 mg/m<sup>2</sup>, weekly) and dexamethasone (20 mg, weekly) as soon as the myeloma diagnosis was established.

#### OUTCOME AND FOLLOW-UP

Unfortunately, the patient died of heart failure during the first cycle of chemotherapy in the third week.

#### DISCUSSION

Multiple myeloma is usually characterized by CRAB symptoms. Bleeding is relatively uncommon in myeloma patients. As reported in a retrospective study<sup>[1]</sup>, the incidence of hemorrhage is 7% in myeloma patients. Men appear to be more affected than women[2-6], most of whom are middle-aged and elderly patients (Table 1). In terms of bleeding sites, not only skin and mucos[1-4,7] but also deep vital organs[8-12] including the gastrointestinal tract, respiratory tract, brain, etc can be involved. Hemorrhagic symptoms can also manifest spontaneously or postoperatively [13-14], occur in isolated sites or multiple sites. With regard to Ig type, a literature review indicated that myeloma patients with IgA type were inclined to bleed [9-10,12,15]. This patient was also IgA-κ type.

The causes of bleeding in myeloma patients are mainly related to thrombocytopenia, hematopoietic failure due to infiltration of plasma cells or hyperviscosity syndrome. Patients rarely present with bleeding symptoms or coagulopathy alone. Our patient initially only presented with recurrent bleeding of oral mucosa and abnormal coagulation function. Factor X deficiency accounted for her coagulopathy. As the disease progressed, immunoglobulinemia, mild anemia, pneumonia, and heart failure were noted. The diagnosis of IgA-к type multiple myeloma was finally confirmed by bone marrow tests and immunofixation electrophoresis.



Table 1 Summary of clinical features in patients with multiple myeloma with bleeding symptoms											
Ref.	Number of bleeding cases/total cases	Gender ( <i>n</i> )	Median/average age (yr)	Types of M protein (%)	Amyloidosis (n)	Bleeding sites	APTT	PT	Π	FIB	Involved coagulation factors ( <i>n</i> )
Kyle <mark>[1</mark> ], China, 2014	3	Male (3)	57	NS	Yes	Skin; Mucous	Prolonged	Prolonged	Prolonged	Ν	XX
Zou <i>et al</i> [2], China, 2002	44636	Male (9); Female (7)	68.9 (average)	IgG (87.5); IgA (6.25); IgD (6.25)	NS	Skin; Nasal mucosa; Gingiva	NS	NS	NS	NS	I, VII, X, Fbg
Zeng <i>et al</i> [ <b>3</b> ], China, 2013	44772	Male (16); Female (14)	60 ± 10 (average)	IgG (90); IgA (6.7);IgD (3.3)	NS	Skin; Nasal mucosa; Gingiva (7)	NS	NS	NS	NS	II, VIII
Xie <i>et al</i> [4], China, 2002	12/358	Male (208); Female (150)	55 (median)	NS	NS	Skin; Nasal mucosa; Gingiva (12)	NS	NS	NS	NS	NS
Zhuang et al[5], China, 2004	20/218	Male (136); Female (82)	57 (average)	IgG (45.3); IgA (18.4); IgD (11.7); IgM (0.6%); к (11.2); λ (9.5); No secretion (2.2); bi- clone (1.1)	Yes (18)	NS	NS	NS	NS	NS	NS
Zhang et al [6], China, 2005	30/148	Male (98); Female (50)	58 (average)	Heavy chain types; IgG (44.7); IgA (22.0); IgM (2); No secretion (31.7); Light chain types; $\kappa$ (47.7%); $\lambda$ (52.3%)	NS	Nasal mucosa (17); Gingiva (7); Melena (6); Hematuria, fundus hemorrhage, gingiva	NS	NS	NS	NS	NS
Sari <i>et al</i> [ <mark>13</mark> ], Japan, 2008	1	Female	43	IgG	NS	Post operation of ovarian cyst	Prolonged	NS	NS	NS	VIII
Dicke <i>et al</i> [ <mark>14</mark> ], China, 2016	1	Male	63	IgG	NS	Post operation of orthodontics	Prolonged	NS	NS	1.8g/l	vWF:Ac
Hobbs <i>et al</i> [ <mark>8</mark> ], USA, 2019	1	Male	59	NS	NS	Gastrointestinal tract	Prolonged	prolonged	NS	NS	Х
Kawashima et al[9], Japan, 2018	1	Male	52	IgA	NS	Thigh muscle, hematuria	Prolonged	Ν	NS	NS	VIII, vWF
Furube <i>et al</i> [ <mark>10</mark> ], Japan, 2018	1	Male	77	IgA	NS	lung	Prolonged	prolonged	NS	NS	NS
Richard et	1	Female	67	IgA	NS	Melena	Prolonged	Ν	Ν	NS	VIII, vWF



Zhang Y et al. Myeloma case presenting coagulopathy initially

al[ <mark>15</mark> ], USA, 1990											
Li <i>et al</i> [ <mark>7</mark> ], England, 1977	1	Male	49	NS	Yes	Mucosa	Prolonged	Prolonged	Prolonged	low	Х
Sun <i>et al</i> [ <mark>11</mark> ], USA, 2001	18/368	Male (221); Female (147)	58	NS	Yes	Gastrointestinal tract, hematuria, skin, spleen, abdomen	Prolonged	NS	NS	NS	X(32)
Zhang <i>et al</i> [12], USA, 2018	1	Male	48	IgA	NS	intracranial	NS	NS	NS	NS	NS

NS: No significance; N: Normal; κ: Kappa; λ: Lambda; APTT: Activated partial thromboplastin time; PT: Prothrombin time; TT: Thrombin time; FIB Fibrinogen.

The main mechanism of coagulation dysfunction in myeloma is believed to involve excessive immunoglobulins which affect coagulation factors, platelets, or fibrinogen, forming protein complexes. These complexes further lead to secondary deficiency of coagulation factors and hemorrhagic symptoms [7,11-12]. Factor II, VII, VIII, X, XI, XI, von W X gen deficiency have been reported in myeloma patients [2-3,16]. As reported, isolated acquired FX deficiency mostly occurs in amyloidosis, and is not so common in myeloma[16-18] (Table 1). In the largest clinical study on acquired Factor X deficiency and amyloidosis, of 368 consecutive patients with systemic light chain amyloidosis, 32 patients (8.7%) had factor X levels lower than 50% of the normal level. Eighteen of these patients (56%) had bleeding complications, which were more frequent and severe in the 12 patients who had factor X levels lower than 25% of the normal level[18]. Earlier studies indicated that the incidence of factor X deficiency in patients with amyloidosis was 6.3% to 14% [19]. With the exception of amyloidosis, isolated acquired factor X deficiency has seldom been reported in other diseases[20]. In this case, we failed to prove the existence of secondary amyloidosis. Before bleeding signs, the patient had cardiac arrhythmia, enlargement of the heart, and progressive heart failure; thus, cardiac amyloidosis was highly suspected. However, this was not proved as a cardiac muscle biopsy was difficult to obtain. Whether isolated acquired factor X deficiency can predict amyloidosis is worth further study.

#### CONCLUSION

Bleeding related to coagulation dysfunction is uncommon in multiple myeloma, especially as the initial manifestation. However, coagulopathy may still be the main complaint in myeloma patients. Many coagulation factors and coagulation inhibitors could be involved in myeloma including factor X. Amyloidosis is a well-recognized cause of isolated acquired factor X deficiency. Whether isolated acquired factor X deficiency can predict the presence of amyloidosis requires further investigation.

#### FOOTNOTES

Author contributions: Zhang Y and Fang Xu F contributed equally to this work; Zhang Y and Xu F designed the study; Zhang Y and Wen JJ collected the data; Zhang Y and Xu F analyzed the data; Zhang Y, Xu F, and Wen JJ interpreted the data; Zhang Y, Xu F, Wen JJ and Shi L prepared the manuscript; Shi L and Zhou QL searched and reviewed the literature.

Informed consent statement: Informed written consent was obtained from the patient for publication of this report.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is noncommercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

Country/Territory of origin: China



WJCC | https://www.wjgnet.com

ORCID number: Ya Zhang 0000-0002-0426-333X; Fang Xu 0000-0002-6731-1116; Jing-Jing Wen 0000-0002-6994-9025; Lin Shi 0000-0002-5259-1290; Qiao-Lin Zhou 0000-0003-0022-0567.

S-Editor: Ma YJ L-Editor: A P-Editor: Ma Y

#### REFERENCES

- 1 Kyle RA. Multiple myeloma: review of 869 cases. Mayo Clin Proc 1975; 50: 29-40 [PMID: 1110582 DOI: 10.1016/S0140-6736(75)91552-4
- Zou Lifang, Hu Junpei, Ye Weide. A Clinical Study of Hemostatic Abnormality in Multiple Myeloma Patients. Xue Shuan 2 Yu Zhi Xue Xue 2002; 8: 118-120
- 3 Zeng Manni. Coagulation factors in patients with multiple myeloma research. Zhonghua Jian kang Wen Zhai 2013; 18-19
- Xie Weicheng, Li Juan, Zhang Guocai, Luo shaokai. Clinical features of 358 cases multiple myeloma. Xin Yi Xue 2002; 33: 4 160-161
- Zhuang Junling, Wu Yongji, Zhong Yuping, He Jian, Shen Ti, Zhang Zhinan. Clinical features of 218 cases multiple 5 myeloma. Zhongguo Shi Yong Nei KeZaZhi 2004; 24: 108-110 [DOI: 10.3969/j.issn.1005-2194.2004.02.025]
- Zhang Jun, Deng Hongyu, Wu Gang, Li Shuangqing. Clinical analysis of 148 cases of multiple myeloma. Clinical Focus 2005; 20: 452-454 [DOI: 10.3969/j.issn.1004-583X.2005.08.014]
- 7 Li Hongmei, Wang Yongjun. Clinical analysis of Multiple myeloma with hemorrhage of digestive tract as initial manifestations. J Clini and Experi Med 2016; 15: 2265-2267 [DOI: 10.3969/j.issn.1671-4695.2016.22.030]
- 8 Hobbs JG, Van Slambrouck C, Miller JL, Yamini B. Intracranial hemorrhage as initial manifestation of plasma cell myeloma: A case report. J Clin Neurosci 2018; 50: 133-135 [PMID: 29428262 DOI: 10.1016/j.jocn.2018.01.054]
- Kawashima I, Takano K, Kumagai T, Koshiishi M, Oishi S, Sueki Y, Nakajima K, Mitsumori T, Kirito K. Combined Coagulopathy Can Induce Both Hemorrhagic and Thrombotic Complications in Multiple Myeloma. Intern Med 2018; 57: 3303-3306 [PMID: 29984746 DOI: 10.2169/internalmedicine.0915-18]
- 10 Furube A, Kagiyama N, Ishiguro T, Takaku Y, Kurashima K, Shimizu Y, Takayanagi N. Diffuse alveolar hemorrhage caused by IgA deposition associated with multiple myeloma. Clin Case Rep 2019; 7: 1049-1052 [PMID: 31110743 DOI: 10.1002/ccr3.2151]
- 11 Sun Mingli, Song Jie, Li Xueyong, Li Yunzhi. Multiple myeloma with special manifestations. J of Leu & Lym 2007; 16: 297-298 [DOI: 10.3760/cma.j.issn.1009-9921.2007.04.023]
- Zhang Xia, Wang Weiwei, Guo Jinjing, Huang Chuanrong, Wang Weiguo. Clinical significance of von Willebrand factor, 12 D-dimer and AT-III in multiple myeloma. Anhui Med J 2018; 39: 456-458 [DOI: 10.3969/j.issn.1000-0399.2018.04.022]
- Sari I, Erkurt MA, Ifran A, Kaptan K, Beyan C. Multiple myeloma presenting with acquired factor VIII inhibitor. Int J 13 *Hematol* 2009; **90**: 166-169 [PMID: 19551464 DOI: 10.1007/s12185-009-0363-9]
- 14 Dicke C, Schneppenheim S, Holstein K, Spath B, Bokemeyer C, Dittmer R, Budde U, Langer F. Distinct mechanisms account for acquired von Willebrand syndrome in plasma cell dyscrasias. Ann Hematol 2016; 95: 945-957 [PMID: 27040683 DOI: 10.1007/s00277-016-2650-x]
- 15 Richard C, Cuadrado MA, Prieto M, Batlle J, López Fernández MF, Rodriguez Salazar ML, Bello C, Recio M, Santoro T, Gomez Casares MT. Acquired von Willebrand disease in multiple myeloma secondary to absorption of von Willebrand factor by plasma cells. Am J Hematol 1990; 35: 114-117 [PMID: 2205095 DOI: 10.1002/ajh.2830350210]
- Liu W, Xuan M, Xue F, Yang R. [Acquired coagulation factor X deficiency: three cases report and literature review]. 16 Zhonghua Xue Ye Xue Za Zhi 2014; 35: 633-636 [PMID: 25052608 DOI: 10.3760/cma.j.issn.0253-2727.2014.07.014]
- Furie B, Greene E, Furie BC. Syndrome of acquired factor X deficiency and systemic amyloidosis in vivo studies of the 17 metabolic fate of factor X. N Engl J Med 1977; 297: 81-85 [PMID: 865580 DOI: 10.1056/NEJM197707142970203]
- 18 Choufani EB, Sanchorawala V, Ernst T, Quillen K, Skinner M, Wright DG, Seldin DC. Acquired factor X deficiency in patients with amyloid light-chain amyloidosis: incidence, bleeding manifestations, and response to high-dose chemotherapy. Blood 2001; 97: 1885-1887 [PMID: 11238135 DOI: 10.1182/blood.V97.6.1885]
- 19 Mumford AD, O'Donnell J, Gillmore JD, Manning RA, Hawkins PN, Laffan M. Bleeding symptoms and coagulation abnormalities in 337 patients with AL-amyloidosis. Br J Haematol 2000; 110: 454-460 [PMID: 10971408 DOI: 10.1046/j.1365-2141.2000.02183.x
- 20 Boudin L, Patient M, Roméo E, Bladé JS, Gisserot O, de Jauréguiberry JP. [Acquired, non-amyloid related factor X deficiency: A first case associated with atypical chronic lymphocytic leukemia and literature review]. Rev Med Interne 2017; 38: 478-481 [PMID: 28110969 DOI: 10.1016/j.revmed.2016.12.003]

WJCC | https://www.wjgnet.com



## Published by Baishideng Publishing Group Inc 7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA Telephone: +1-925-3991568 E-mail: bpgoffice@wjgnet.com Help Desk: https://www.f6publishing.com/helpdesk https://www.wjgnet.com

