ANTIPHOSPHOLIPID SYNDROME AND THROMBOSIS

Petr Dulíček
IVth Internal Clinic, Department of Hematology, University Hospital and Medical Faculty, Hradec Králové

We describe a case report of male with incidental finding of lupus anticoagulant antibody and deep vein thrombosis after surgery. Recurrent thrombosis developed shortly after the cessation of thromboprophylaxis. It was very difficult to keep INR within the therapeutic range. However, therapy was complicated by hair loss and extension of thrombosis. So that rivaroxaban was introduced and resulted in recanalisation of vein. We recommend a long term anticoagulation therapy.

Key words: lupus anticoagulans, venous thromboembolism, rivaroxaban.

Introduction
Detection of prolonged aPTT before surgery is always associated with surgeons worries about an increased risk of bleeding. Hematologist play a role in rapid clarification of prolonged aPTT and in the case of lupus anticoagulans, pharmacological prophylaxis is indicated. In the presence of clinical symptoms (DVT in this case), the criteria for antiphospholipid syndrome (APS) are fulfilled.

APS is associated with an increased risk or recurrence. Rivaroxaban (Xarelto) is direct inhibitor of FXa and since 2012 has been available for therapy of venous thromboembolism (VTE) (I). However, there is not too many data about therapy of VTE in patients with APS concerning efficacy and safety. Current data are variable.

Case report
52 y. old Caucasian male was admitted in December of 2007 y. to Neurosurgery Clinic for operation of cervical spine column.

Family history was completely negative concerning VTE. Personal history was until admission also unremarkable and he was annually checked in general practitioner.

He also passed couple of teeth extractions without an increased bleeding. He decided to visit Grand Canaria at September 2016 and he suffered from head injury. The wave took him away from sea to seashore and he was shocked for a while. He could not move with right upper extremity for 10 minutes. After arrival to Czech Republic he visited the orthopedists and neurologists. X-ray of cervical and thorax spine did not reveal any pathology. The rehabilitation and massages were recommended together with intake of vitamins. This therapy led to only contemporary relief of pain and therefore CT scanning was indicated.

Unstable fracture of C6/C7 was found, fortunately without injury of spine column. Neurosurgeon indicated the operation. Routine examination before the admission was completely normal in the term of WBC, X chest-ray and biochemistry. Coagulation work-up has not been done due to the negative family and history of bleeding tendency. Prothrombin time (PT) and activated partial thromboplastin time (aPTT) were done after admission. PT was normal, but aPTT was significantly prolonged (patients time 76.1s / 33.9 s of control plasma), with ratio 2.24. Test was repeated with the aim to exclude an error, but the result was the same.

Hematologist was called at the patients immediately and following questions were put.
1) is it possible to make an operation next day after administration of plasma and laboratory control
2) if the patient is predisposed towards the bleeding
3) if thromboprophylaxis with LMWH is indicated.

Hematologists gave an advice to postpone surgery and to explain the etiology of prolonged aPTT. The surgery was 1 day put off and the first step was to LA (lupus anticoagulant) work-up. aPTT was even more prolonged with reagent sensitive to LA and suspicious of LA was even stronger. LA was further confirmed with confirmatory tests.

Hematologists indicated thromboprophylaxis with LMWH after surgery and no administration fresh frozen plasma. Surgery was made.

CORRESPONDENCE ADDRESS OF THE AUTHOR: Doc. MUDr. Petr Dulíček, Ph.D., PetrDulicek@seznam.cz
IVth Internal Clinic, Department of Hematology, University Hospital and Medical Faculty, Hradec Králové
Sokolská 581, 500 05 Hradec Králové

Translated from: Klin Farmakol Farm 2016; 30(1): 42–43

Tab. 1. Coagulation work-up is shown in the table 1

<table>
<thead>
<tr>
<th>Test</th>
<th>Patient time</th>
<th>Control time</th>
<th>Ratio</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT</td>
<td>14.2</td>
<td>14.3</td>
<td>1.0</td>
<td>0.8–1.25</td>
</tr>
<tr>
<td>aPTT</td>
<td>33.9</td>
<td>76.1</td>
<td>2.24</td>
<td>0.9–1.2</td>
</tr>
</tbody>
</table>
without any complications and after one week the patient was transferred to district hospital with the goal of intensive rehabilitation. LMWH was stopped, but after 4 days of withdrawal the pain in left calf developed.

The calf became a little bit swollen.

Doppler US detected acute thrombosis in popliteal vein. After hematologists consultation, LMWH was introduced in therapeutic dose with the switching into warfarin. INR was difficult to keep in therapeutic range (2–3) and what was even worse, patient complained about hair loss. GP decided to bring warfarin to an end.

The patient was OK until March of 2013, when he visited Emergency Dept. US detected a new deep vein thrombosis in femoropopliteal vein of left extremity.

This time rivaroxaban was started in standard dose 2 x 15 mg and after 3 weeks we continued with dose 20 mg once daily. Anticoagulant therapy was tolerated well, without bleeding complications (2). US of affected leg was repeated after one year and veins were patent. Because of increased risk of recurrence of thrombosis in patients with APS, we decided to carry on rivaroxaban.

Discussion

All causes of prolonged aPTT is considered as increased risk of bleeding in daily clinical praxis. However, it is well known fact, that it’s not always true. Detection of LA belongs also to these situations. On the contrary, the increased risk of thrombosis, either arterial, or venous is presented. After acute thrombotic episode LMWH + warfarin are considered as "gold standard", in spite of the fact, that INR is not always easy to manage within therapeutic range. Hair loss was another complication, so that we decided to indicate rivaroxaban. We were aware of sparse data about efficacy and safety in this scenario (3, 4). The therapy was well tolerated with the benefit of no necessity to laboratory control. Veins became patent in control US after one year. We did not await such a therapeutic success. Nowadays, some clinical trials are ongoing on this topic (5).

Summary

We think, that this case report is interesting from these points of view.

1) Prolonged aPTT is not automatically associated with increased risk of bleeding. In case of LA is an opposite tendency.

2) Thromboprophylaxis with LMWH is indicated in all well-known risk situations for VTE.

3) INR can be more difficult to manage in the therapy with warfarin.

4) One rare complication – hair loss occurred in our patient.

5) Therapy of VTE with rivaroxaban in APS is not clear yet in the term of efficacy and safety.

6) Therapy was successful in our case but after one year we have to solve the difficulty with rivaroxaban. This therapy is paid only one year after VTE event.

7) LMWH was chosen instead of rivaroxaban.

Conclusion

We described case report of male with APS and acute proximal deep vein thrombosis. Therapy with rivaroxaban was successful, without any adverse effects, but the problem arises after one year, when patient is not able or willing to pay this therapy.

REFERENCES


Tab. 2. The results are shown in Table 2

<table>
<thead>
<tr>
<th>Test</th>
<th>Patient</th>
<th>Control</th>
<th>Ratio</th>
<th>Normal range</th>
<th>Correction after 1 and 2 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT</td>
<td>14.1</td>
<td>14.0</td>
<td>1.0</td>
<td>0.8–1.25</td>
<td>75/74</td>
</tr>
<tr>
<td>aPTT</td>
<td>81.1</td>
<td>34.5</td>
<td>2.35</td>
<td>0.9–1.2</td>
<td>95.1/95.5</td>
</tr>
<tr>
<td>aPTT na LA</td>
<td>131.1</td>
<td>35.4</td>
<td>3.7</td>
<td>0.9–1.2</td>
<td>95.1/95.5</td>
</tr>
<tr>
<td>dRVVT</td>
<td>42.6</td>
<td>29.9</td>
<td>1.42</td>
<td>0.9–1.2</td>
<td>39.9/38.5</td>
</tr>
<tr>
<td>TT</td>
<td>13.8</td>
<td>13.8</td>
<td>1.0</td>
<td>0.9–1.2</td>
<td></td>
</tr>
</tbody>
</table>