Treatment of recurrent gastrointestinal haemorrhage in a patient with von Willebrand’s disease with administration of octreotide LAR and propranolol

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ABSTRACT
We report a patient with von Willebrand’s disease who had had recurrent and life-threatening bleeding from the gastrointestinal tract. Despite extensive investigation, no apparent cause of haemorrhage was identified. He was successfully treated with combined administration of octreotide LAR (long-acting release) and propranolol. This is the first report on the successful use of octreotide LAR in a patient with von Willebrand’s disease.

Keywords: Gastrointestinal haemorrhage, Von Willebrand’s disease, Octreotide LAR

INTRODUCTION

Von Willebrand’s disease (vWD) is the most common inherited bleeding disorder. It is caused by quantitative deficiency or qualitative abnormalities of von Willebrand factor (vWF). It is usually an autosomal dominant disease and less frequently an autosomal recessive one, although acquired forms have also been reported. vWD has been classified into three types: Type I, accounting for 70-80% of patients, represents a quantitative deficiency of vWF; Type II, accounting for 13-18% of patients, is characterized by several qualitative abnormalities of WF; and Type III, accounting for 1-3% of patients, is characterized by undetectable levels of vWF. Clinical presentation is variable, depending on the type. In types I and II, manifestations include bleeding from mucosal surfaces (epistaxis, bleeding from the gastrointestinal tract and menstrual bleeding), and bleeding with dental extractions or surgical procedures, whereas in type III bleeding mimics the findings seen in hemophilia, including joint bleeding. Diagnosis of vWD should be considered in patients with a personal and family history of bleeding episodes and is established with the following laboratory findings: a) prolonged bleeding time, b) moderately prolonged activated partial thromboplastin time, c) absence of ristocetin-induced platelet aggregation, d) decrease of factor VIII, and e) decrease of vWF antigen and vWF activity.2

Treatment of patients with vWD depends on the bleeding manifestations and disease type. Until re-
cently, treatment of bleeding from the gastrointesti-
nal tract in patients with vWD included administra-
tion of tranexamic acid, red cell transfusion, intrave-
nous clotting factor products such as fresh frozen pla-
ma and cryoprecipitate (which contains 5-10 times
more vWF and FVIII than fresh frozen plasma), and
purified vWF concentrates or preparations that con-
tain vWF and FVIII[1,2]. Desmopressin, which promotes
the release of vWF from endothelial cell storage sites
in mild forms of vWD, has also been used[3], as well as
beta-blocking drugs, which cause a reduction in por-
tal pressure[4], hormonal therapy with estrogen with or
without progesterone[5], immunoglobulin in acquired
forms of vWD[2] and surgical resection of lesions that
have been clearly identified as the source of bleeding[4,5].

We report a patient with vWD who has had recur-
rent and life-threatening bleeding from the gastrointesti-
nal tract, in whom, despite an extensive in-
vestigation, no apparent cause of haemorrhage was
identified. He was successfully treated with combined
administration of octreotide LAR (long active re-
leased) and propranolol. This is the first report on
the use of octreotide LAR in a patient with vWD.

CASE REPORT

A 55-year old man presented to our Department
because of recurring episodes of melaena, which had
first appeared five years previously. During the in-
vestigation of his bleeding diathesis, he was found to
have type I vWD. He had a history of epistaxis during
his childhood. His niece was also diagnosed with type
I vWD, whereas his father, brother and grandmother
suffered from bleeding diathesis but no specific in-
vestigation had been undertaken. Laboratory investi-
gation was compatible with the diagnosis of vWD, with
prolonged bleeding time (15 min, normal range 3-8
min), moderate prolongation of activated partial
thromboplastin time (41 sec, normal range 20-30 sec),
mild deficiency of FVIII (42%, normal range 50-
150%), complete absence of ristocetin-induced plate-
let aggregation, moderate decrease of vWF (29%,
normal range 50-160%) and a moderate decrease of
vWF antigen (33%, normal range 50-160%). The di-
agnosis of type I vWD was based on the findings of
prolonged bleeding time, moderate prolongation of
activated partial thromboplastin time, as well as mo-
derate decrease of vWF, moderate decrease of vWF
antigen and mild deficiency of FVIII. Platelet count
(300,000/μL) and prothrombin time (12 sec) were with-
in normal limits and an extensive laboratory investiga-
tion excluded the presence of concomitant disor-

ders.

During the past 17 months, the patient had been
admitted 14 times for recurrent episodes of melaena
with an overall hospitalized time of 98 days and con-
sequent long sick leaves from his job. On two occa-
sions, hemoglobin concentration on admission was 6
g/dL. He required 40 red cell transfusions and 22,000
IU of purified vWF. During this period, upper endo-
scopy was performed five times, small bowel series
radiography twice and colonoscopy three times; com-
puted tomography of the abdomen, radionuclide scan-
ing with 99mTc pertechnetate-labeled autologous red
blood cells, angiography of the superior mesenteric
artery and exploratory surgery with intraoperative
enteroscopy were also performed, but the source of
bleeding could not be localized. He had received in-
tranasal desmopressin for three months with no ef-
fect on the frequency of bleeding. He was subsequently
treated with octreotide LAR 20mg (Sandostatin LAR,
Novartis, Athens, Greece) IM once a month, along
with propranolol 20mg per os three times per day.
With this therapeutic regimen the bleeding stopped
completely, the hemoglobin values stabilized at nor-
mal levels (13.2 g/dL) and no treatment-related side
effects were observed. During a follow-up period of
eight months, bleeding did not recur and the patient
has returned to his work. Repeated evaluation of vWD
revealed that vWF levels did not rise (28%), ristoce-
tin-induced platelet aggregation remained absent and
activated partial thromboplastin time and bleeding
time prolongations remained unchanged.

DISCUSSION

We have shown that recurrent bleeding from the
gastrointestinal tract can be successfully managed with
the combined administration of octreotide LAR and
propranolol. We must point out that no apparent
source of bleeding could be determined and the haem-
orrhage could not be controlled with appropriate treat-
ment applied for many months (red cell transfusions,
administration of desmopressin and vWF), while sur-
gical treatment was not applicable since the source of
bleeding could not be located.
Octreotide is mainly used in acromegaly and in gastrointestinal and pancreatic tumors. Nevertheless, octreotide has been proved to be effective in controlling bleeding from the gastrointestinal tract due to angiodysplasia and variceal bleeding. It is postulated that it exerts its actions through a reduction in splanchic and portal blood flow. Octreotide LAR, compared to conventional octreotide, has the advantage that it is administered once monthly and does not require hospitalization while exhibiting a similar efficacy and safety profile.

Only one report on the effectiveness of octreotide therapy in two patients with vWD was found in the literature. In these two patients angiodyplasias located in the stomach, duodenum and small bowel were detected. In our patient, no angiodyplasias were found despite an extensive work-up. Wireless capsule endoscopy is currently the gold standard for the diagnosis of small intestine angiodyplasias; unfortunately, this technique is not available in our Hospital. Therefore, the possibility of an unrecognized angiodyplasia, which could have been the source of gastrointestinal bleeding in our patient, still exists. Finally, in one of the previously reported patients, vWF was increased after the administration of octreotide. In our patient octreotide did not cause any increase in the synthesis or release of vWF.

Undoubtedly, more trials are required in order to clarify the mechanism of action of octreotide in this setting. Whatever the mechanism involved, combined administration of octreotide and propranolol appears to be an attractive alternative treatment in these rare and life-threatening conditions, when other therapeutic modalities have failed.

REFERENCES

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