The Canadian Experience: Severe Factor V Deficiency

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Background:

- Severe Factor V deficiency (sFVD) is a rare congenital bleeding disorder associated with FV of 1 U/dL and autosomal recessive inheritance.
- It is typically associated with spontaneous bleeding, particularly involving skin and mucosal surfaces.
- With no specific FV-containing concentrate available, fresh frozen plasma (FFP) is the standard product used for treatment and prophylaxis.
- The Canadian Hemophilia Registry (CHR) reports 6 patients with sFVD among the Canadian population of 34 million.

Objective:

To describe bleeding manifestations and treatment of sFVD in Canada

Methods:

- Retrospective chart review of 5 patients with sFVD identified through CHR

Results:

Patient demographic information and description of bleeding manifestations are included in Table 1.

- The majority of patients are Caucasian with none reporting a family history.
- Diagnosis of sFVD occurred in these individuals after investigation of prolonged provoked bleeding or menorrhagia.
- Two patients have been genotyped with both identified as compound heterozygotes.
- FFP has been used as treatment/surgical prophylaxis for the majority of bleeding episodes with adequate FV recovery.
  - Two patients required antihistamines prior to FFP due to allergic reactions.
- Adjuvant therapies used include tranexamic acid and desmopressin.
- One patient received recombinant activated Factor VII (rFVIIa) and prothrombin complex concentrate (PCC) due to religious beliefs.

Table 1: Description of patient demographics and bleeding manifestations

Case	Age (Yrs)	Sex	Age at Diagnosis	Genotype	Bleeding Symptoms	Treatment	FV Recovery (IU/dL)	FFP Reactions	Procedures
1	4.5	M	2.5 years	Exon 13 deletion / Exon 22 G2060D	Traumatic Frenulum, Tongue	FFP 15-20mL/kg, TXA	31 post 22mL/kg FFP	N/A	FFP prophylaxis with dental procedures
2	21	F	13 years	Exon 15 Y1702C / Exon 17 V1813M	Bruising, Epistaxis, Menorrhagia, Traumatic Rt Calf	FFP 15-20mL/kg, TXA, DDAVP (menorrhagia)	33 post 6U FFP	HTN, nausea, headache, mild SOB	FFP prophylaxis at C-section
3	23	F	19 years	N/A	Postpartum Hemorrhage	Nil	N/A	Nil	Uncomplicated second pregnancy with no FFP prophylaxis
4	23	M	5 days	N/A	Post circumcision Spontaneous Rt Psoas, Rt Gluteal (2) Traumatic Lt Forearm	FFP 10-20mL/kg, TXA, rFVIIa, PCC	19 post 3U FFP	Nil	FFP prophylaxis with dental procedures
5	28	F	7 months	N/A	Epistaxis, Menorrhagia Multiple Spontaneous/Traumatic Hemarthrosis, Rt Iliopsoas (2) Hemorrhagic ovarian cysts	FFP 15-20mL/kg, TXA	22 post 4U FFP	Hives	FFP prophylaxis with dental procedures

Abbreviations: M – Male, F – Female, FFP – Fresh Frozen Plasma, TXA – Tranexamic Acid, DDAVP – Desmopressin, rFVIIa – Recombinant Activated Factor VII, PCC – Prothrombin Complex Concentrate, U – Units, Rt – Right, Lt – Left, HTN - Hypertension

Conclusions:

1. BLEEDING MANIFESTATIONS:

- The majority of bleeding symptoms experienced by the patients described involved mucosal surfaces although two patients in this case series also experienced spontaneous musculoskeletal bleeding similar to that seen in severe congenital hemophilia.
- Females require particular attention to the management of gynecological bleeding (i.e. menorrhagia, hemorrhagic ovarian cysts, peri/postpartum bleeding).
- Three pregnancies were carried to term in two of the female patients; one received prophylaxis with FFP beginning prior to and for four days after delivery with no complications while the other patient did not receive prophylaxis with two deliveries and experienced an immediate postpartum hemorrhage with one delivery.

2. MANAGEMENT:

- In these patients, FFP 15-20mL/kg has been effective in achieving hemostatic levels of FV (>0.20 U/mL) with minimal AE and remains the mainstay of therapy.
- Nonetheless, the development of a recombinant FV concentrate to provide more optimal management of serious bleeding experienced by these patients is needed in order to prevent complications associated with the use of large volumes of FFP often needed for these patients and to allow more accurate FV recovery.

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