

## IWWM-10 Poster Presentations, Friday, October 12, 2018, Gamble

### W11: A single centre case series of patients with Waldenstroms Macroglobulinaemia and Acquired von Willebrand Syndrome

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#### Introduction

We present a case series of six patients with Waldenströms Macroglobulinaemia (WM) and acquired von-Willebrand's syndrome (AVWS) at a District General Hospital in the UK. AVWS has previously been reported to be rare complication of WM, although Castillo et al\*, recently presented a larger retrospective study of 320 WM patients with 15% having AVWS (ASH 2017). The International Society for Thrombosis and Haemostasis (ISTH) defines AVWS as a von willebrand factor (vWF) activity level of  $<0.3\text{iu/ml}$  or  $<30\text{iu/dl}$ . The entity of low vWF levels is classified between  $0.3 < 0.5\text{iu/ml}$  or  $30 < S0\text{iu/dl}$ . The ISTH has an international registry of 186 AVWS cases, of these 16 cases (9 %) were secondary to WM'. The prothrombin time (PT) should be normal and the activated partial thromboplastin time (APTT) may be normal or only slightly prolonged if the Factor VIII is also reduced, so are not useful 'screening tests' for AVWS. Historically, patients at our site were screened for AVWS if a typical bleeding history (mucocutaneous and/or gastrointestinal) or significantly deranged clotting screens. However in view of recent data, in the last 6 months all patients have been screened prior to bone marrow biopsy.

#### Materials & Methods

Factor VIII testing was performed by a one stage Activated Partial Thromboplastin based assay using HemoSIL Reagents on an ACL TOP700 analyser. Von Willebrands Antigen was performed using HemoSIL vWF Ag immunoturbidometric latex agglutination assay on the ACL TOP700 analyser. Von Willebrands Activity was performed using HemoSIL vWF Activity assay on the ACL TOP700 analyser, using polystyrene latex particles coated with a purified anti-vWF mouse monoclonal antibody directed against a functional epitope of vWF.

#### Results

We have identified 9% of our WM cohort (6 out of 69) meeting criteria for AVWS or low level vWF levels. The mean FVIII level of patients was  $37.7\text{iu/dL}$  ( range  $26.3 - 55.1\text{iu/dL}$ ). The mean vWF antigen level was  $31.4\text{iu/dL}$  (range  $18.9 - 40.6\text{iu/dL}$ ). The mean vWF activity level was  $25.3\text{iu/dL}$  (range  $9.8 - 37.2\text{iu/dL}$ ). Of note all these patients had high total IgM levels of  $>50\text{g/l}$ . This is in keeping with the Daner-Faber cohort' of the strong correlation with high IgM levels and AVWS. Clinical features are listed in *table 1*.

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### **Conclusion**

This series provides further evidence that AVWS is higher than previously reported in WM and warrants a larger prospective registry based study to investigate the incidence in WM, Furthermore, we would recommend screening for AVWS in all patients with known WM or under investigation prior to invasive procedures such as bone marrow biopsy.

### **References**

1. Castillo J et al Acquired Von Willebrand Disease in Patients with Waldenström Macroglobulinemia. Blood 2017 130:1088
2. Federici AB et al Acquired von Willebrand syndrome: data from an international registry. Thromb Haemost 2000 Oct;84(4):739.

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Table 1: Laboratory and clinical features at diagnosis, including International Prognostic Scoring System for Waldenstroms Macroglobulinaemia (ISSWM)

\* (low/intermediate/high risk score)

Patient	Symptoms	Total Protein (60-80g/L)	Total IgM (0.5-2.0g/L)	IgM Para-protein (g/L)	SFLC (mg/L)	Plasma viscosity (1.5-1.72mPa.s)	FVIII (50-200iu/dL)	VWF activity (50-200iu/dL)	VWF antigen (50-200iu/dL)	PT (10.2-12.60s)	APTT (24.80-35.6s)	ISSWM*
1	Rectal bleeding requiring transfusion	109	90.4	52.6	K 23.4 h 442 ratio 3.2	n/a	29.5	14.9	22.2	16.2	46.2	Int
2	No hyperviscosity Increased bleeding with minor injury	95	»58.5	32.3	K 49.5 h 7.6 ratio 6.5	4.74	40.8	36.7	40.6	14.8	49.3	Int
3	No hyperviscosity or bleeding symptoms	99	»58.5	36.7	K 814 h 6.6 ratio 123	4.23	36.8	24.9	28.9	11.1	40.6	High
4	No hyperviscosity or bleeding symptoms	100	>58.5	25.8	K 270 h 9.3 ratio 29.0	n/a	55.1	28.2	37.5	12.2	36.2	High
5	Hyperviscosity with headaches and blurred vision	91	50.3	22.5	K 9.5 h 44.2 ratio 0.21	2.72	37.6	37.2	40.4	10.8	35.10	Int
6	No hyperviscosity or bleeding symptoms	111	»58.5	36.6	K 31.0 h 9.4, ratio 3.3	8.02	26.3	9.8	18.9	12.80	43.10	Low