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901.HEALTH SERVICES AND QUALITY IMPROVEMENT - NON-MALIGNANT CONDITIONS

A Single Center Experience of 13 Episodes of Acquired Hemophilia A (2019 - 2023)

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Background: Acquired Hemophilia A (AHA) is a rare bleeding disorder caused by neutralizing autoantibodies to factor VIII (FVIII). Treatment of AHA involves immunosuppression to eliminate the autoantibody and hemostatic management involving bypassing agents (BPAs). While the use of BPAs, including activated prothrombin complex concentrate (aPCC) and recombinant activated factor VII (rFVIIa), is primarily derived from studies of congenital hemophilia with inhibitors, registry studies of AHA have also demonstrated the efficacy of rVIIa (*Baudo et al., Blood, 2012*) and aPCC (*Borg et al., Haemophilia, 2015*) (*Zanon et al., Br J Haem 2019*). Given the changing treatment landscape, low incidence of AHA, and high morbidity and mortality associated with the disease, our study aims to describe a single institution's experience with treating AHA.

Methods: We retrospectively reviewed the records of adult patients diagnosed with AHA at a single academic medical center between January 1, 2019, and June 30, 2023.

Results: Eleven patients were treated for 13 distinct episodes of AHA, with one patient admitted for three discrete episodes of AHA with responses to therapy followed by relapses once lost to follow-up. The patients were predominantly white (63.7%, n=7) and female (63.7%, n=7), with a median age of 74 years and weight of 87 kg on admission (Table 1). One patient (9.1%) had concomitant autoimmune disease. No patients presented peripartum or with active malignancy, liver disease, or a family history of bleeding disorders. The median FVIII level on admission was 1% (IQR=1%, 3.5%), with a median anti-FVIII antibody titer of 27 BU (IQR=4.5 BU, 47 BU). Given mild bleeding presentation, Patient 2 was treated as an outpatient with immunosuppression only.

All patients received aPCC as the first-line BPA. Patient 5 developed uncontrolled bleeding from an arterial line despite receiving aPCC and was transitioned to rFVIIa for two days before resuming aPCC once hemostasis was achieved. The median duration of aPCC therapy was eight days. The use of aPCC (FEIBA) instead of rFVIIa (NovoSeven) as the first-line BPA led to total estimated cost avoidance of $13.5 million (calculated using average wholesale price). No patients had thrombotic events after the diagnosis of AHA.

Six episodes (46.1%) were treated with prednisone and rituximab. Six episodes (46.1%) were treated with prednisone and oral cyclophosphamide. One episode (7.7%) was treated initially with prednisone and cyclophosphamide but was eventually transitioned to rituximab following a lack of response and bleeding complications after two weeks. This patient was also subsequently treated with emicizumab for five months until FVIII activity was recovered.

P neumocystis jirovic i i pneumonia prophylaxis was prescribed in eight episodes (61.5%), and antiviral prophylaxis was prescribed in one episode (7.7%). No infections were noted during the follow-up period, other than two documented cases of COVID-19, one of which required admission.

The median time to achieve FVIII >50% was 5.1 weeks, with a median of 8.6 months of follow-up (Figure 1). Patient 11 relapsed twice, as described in Table 1. No other patient relapsed during the follow-up period. No patient deaths occurred during the follow-up period.

Conclusions: We describe 13 episodes of AHA successfully treated at a single academic medical center between 2019 and 2023. aPCC was the first-line BPA administered in all patients, with significant cost savings relative to rFVIIa. Immunosuppression, including prednisone and either cyclophosphamide or rituximab, was used to successfully eliminate autoantibodies in all patients. One patient received emicizumab for ongoing hemostatic control until achieving improvement in FVIII activity. No significant infections, thrombotic events, or deaths were noted in this cohort.

Disclosures Streiff: *Pfizer:* Consultancy; *Bristyol Myers Squibb:* Consultancy; *CSL Behring:* Consultancy.

Table 1: Baseline Characteristics at Presentation												
Episode #	Age (yr)	Sex	Race	Weight (kg)	Admission Length (d)	Bleeding Type	Factor VIII Level (%)	Anti-Factor VIII (BU)	Hgb (g/dL)	Platelets (x10^9/L)	PT (seconds)	APTT (seconds)
1	64	F	Black	61.7	21	Cutaneous	4	96	9.9	288	10.3	53.4
2	73	F	White	80.6	N/A	Gastrointestinal	1	4	14.1	330	N/A	N/A
3	75	M	White	76.6	7	Deep Muscle	1	30	7.4	289	11.4	68.7
4	76	M	White	107.9	64	Cutaneous	1	57	6.1	179	12.4	70.2
5	75	F	Black	103.8	27	Gastrointestinal	1	246	7.7	415	10	65.2
6	87	F	White	103.7	13	Gastrointestinal	1	6	7.3	106	9.2	65.9
7	77	M	White	99.7	21	Cutaneous	3	24	7.7	269	8.7	74
8	70	M	White	84.6	7	Cutaneous	<10[a]	0[b]	9	996	9.8	26.1
9	82	F	Black	82.2	11	Deep Muscle	6	4	8.6	N/A	11	38.1
10	57	F	White	131.4	9	Cutaneous	3	37	7.2	322	10.3	41.3
11[c]	25	F	Black	89.4	9	Deep Muscle	1	30	8	218	9.3	52.3
12[c]	26	F	Black	75	19	Cutaneous	1	5	8.4	51	11.6	40.7
13[c]	27	F	Black	108	15	Deep Muscle (biopsy-related)	6	4	7.1	72	12.3	56.9

[a]Chromogenic FVIII level (given discordance between one-stage FVIII assay and Chromogenic FVIII assay)

[b]Presumed to be inhibitor not detected by assay

[c]Episodes 11, 12, and 13 are for the same patient. These are 3 discreet episodes of relapse, with loss of follow-up in between.
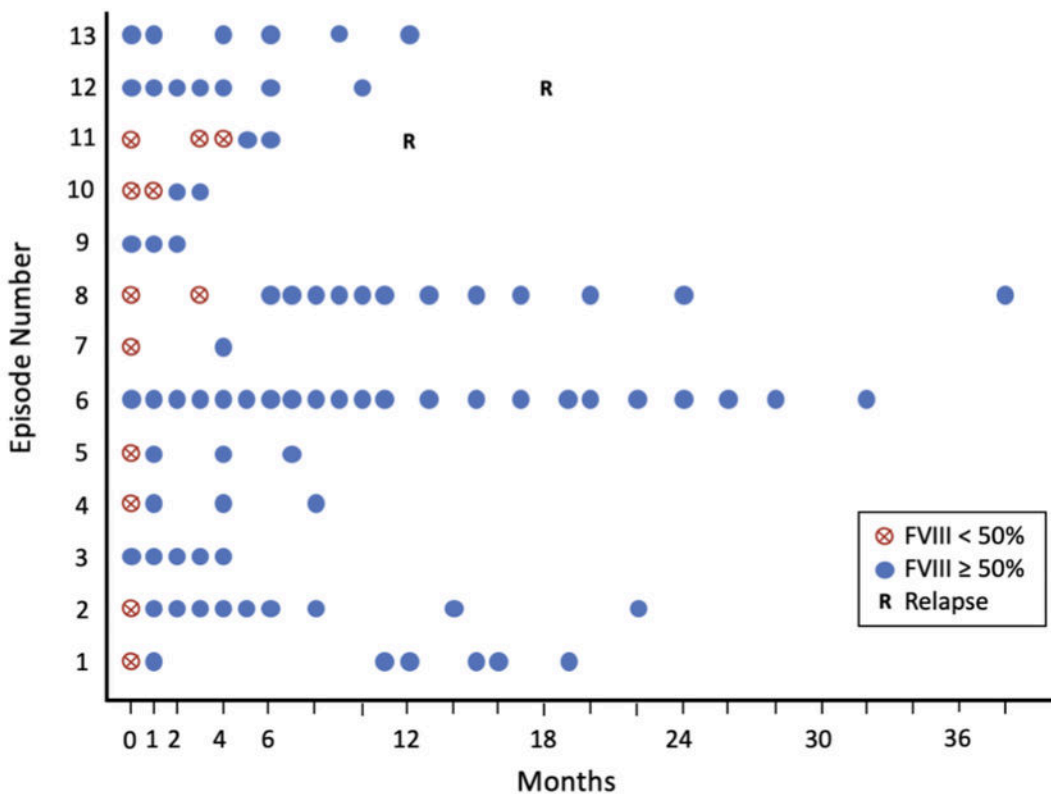

Figure 1: Clinical course and response to therapy

Figure 1