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Clinical Features of Vaccine-induced Immune Thrombocytopenia and Thrombosis (VITT)

Supplementary Tables and Figures

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Table S1: Missing data or unfulfilled clinical or laboratory features of the probable and possible cases

Clinical laboratory features at presentation	Outside defined time limits after ChAdOx1 nCov-19 vaccine	Platelets >150 x10^9/L	No documented thrombosis	D dimers Not sufficiently raised	Anti-PF4 Ab negative
Probable (n=50 patients)					
Unfulfilled criteria	1 VTE presented at 48 days 5 VTEs at 30-42 days	2*	6 **	0	6
Missing data	1	2	0	18	16
Possible (n=17 patients, 34 data points)					
Unfulfilled criteria	1 VTE presented at 52 days	3	0	5	3
Missing data	0	0	1	15	6

*these two cases had low normal platelet counts (153 and 173), it is unknown whether they had dropped from previously higher levels.

Table S2: Medical and relevant drug history in patients with VITT

Condition/Medication number (% of total cohort of 165 where this is known)	Detail
Autoimmune disease 14 (8%)	Autoimmune hepatitis (2), connective tissues disease (2), immune thrombocytopenic purpura (1), Crohn's disease (2); sarcoidosis (1), myasthenia gravis (1), Guillain-Barre syndrome (1) and hypothyroidism (4).
Cancer 4 (2%)	Melanoma, breast, thyroid and vulvar carcinoma
Prior venous thromboembolism 4 (2%)	DVT (2), PE (2). Presentation of VITT associated with recurrent VTE (1), CVST (1), limb ischaemia (1) and renal infarction (1).
Prothrombotic disorders 2 (1%)	None with known thrombophilia or antiphospholipid syndrome. Two had myeloproliferative disease (presented with CVST and VTE respectively).
Hormonal preparations 11 (6%)	Combined contraceptive pill (3), progesterone only pill (5) hormone replacement therapy (3)
Anticoagulants/antiplatelet agents 12 (7%)	Apixaban (4), rivaroxaban (2), warfarin (1), Aspirin (4), clopidogrel (1)
Arterial risk factors 31 (19%)	Diabetes (8), smoking (8), hypertension (7), obesity (12), history of angina or stroke (3). Presentation of VITT associated with arterial disease in 5 (16%); four with ischaemic limb and one with aortic thrombosis.
Known COVID-19 infection 3 (2%)	3 in the previous 3 months, none current
Other documented past history 29 (17%)	Asthma (6), migraines (5), mental health disorders (13) and alcoholic liver disease (5)

Table S3: Clinical characteristics according to presenting thrombosis

Site of thrombosis or haemorrhage	Number (%)	Age median (IQR)	Sex: Female (%)	Days from vaccine median (IQR)	Presenting platelet count x10^9/L Median(IQR)	Presenting fibrinogen g/L median (IQR)	Presenting D dimer (/1000) FEU median (IQR)
CVST	110 (50)	48 (34 to 55)	66 (60)	13 (10 to 16)	41 (22 to 67)	2.0 (1.3 to 3.0)	20 (8 to 38)
CVST with platelets<30	34 (15)	46.5 (34 to 49)	22 (65)	13 (10 to 15)	19 (14 to 22)	1.5 (1.0 to 2.1)	33 (18 to 59)
Missing data N (%)		0	0	0	1	4	4
CVST with Platelets >30	76 (35)	50 (33 to 57)	42 (55)	12 (10 to 17)	53.5 (40 to 89)	2.3 (1.4 to 3.1)	17 (5 to 34)
Missing data N (%)		1	1	1	0	2	9
ICH	42 (19)	51 (39 to 57)	30 (71)	13 (10 to 16)	34 (22 to 64)	1.8 (1.1 to 2.9)	25 (11 to 35)
Missing data N (%)		0	0	1	0	2	7
DVT and/or PE	82 (37)	48 (39 to 56)	40 (49)	14 (11 to 17)	49 (31 to 79)	2.0 (1.2 to 3.5)	20 (10 to 38)
Missing data N (%)		1	0	1	0	6	3
PVT and/or other splanchnic vein thrombosis	41 (19)	47 (36.5 to 49.5)	23 (56)	13.5 (11 to 15.5)	34 (14 to 64)	2.1 (1.3 to 2.5)	23 (10 to 54)
Missing data N (%)		1	0	0	0	3	1
Adrenal thrombosis and haemorrhage	6 (3)	62 (46 to 66)	3 (50)	15.5 (12 to 21)	58.5 (34 to 85)	3.0 (2.1 to 4.1)	10 (5 to 31)
Missing data N (%)		0	0	0	0	0	0
Limb ischaemia or aortic thrombus	26 (12)	56 (48 to 61)	13 (50)	14 (11 to 15)	45.5 (21.5 to 72.5)	2.4 (1.5 to 3.0)	20 (4 to 27)
Missing data N (%)		1	0	0	0	3	6
Cardiac or cerebrovascular event	26 (12)	46 (39 to 50)	14 (54)	11 (8 to 14)	52 (36 to 74)	2.6 (1.8 to 3.1)	20 (11 to 28)
Missing data N (%)		0	0	0	0	4	2
Thrombosis in multiple vascular beds	64 (29)	47 (40 to 55)	33 (52)	13 (10 to 15)	42.5 (22 to 79)	2.1 (1.2 to 3.0)	20 (8 to 38)
Missing data N (%)		1	0	0	0	6	7

Table S4: Comparison of presenting features by thrombotic site for patients with VITT

Presenting variable	CVST (n=110)	Isolated PE (n=31)	Arterial (n=47)
Days from vaccine	5-31 (13)	8-48 (15)	6-75 (12)
Age years	18-73 (48)	21-77 (48)	21-78 (47)
Platelet count $x10^9$/L	6-190 (45)	9-149 (49)	6-222 (43)
D dimer (/1000) FEU	2-80 (30)	0.5-80 (25)	1-138 (20)
Fibrinogen g/L	0.3 – 5.2 (2)	0.7-6.0 (2.5)	0.7 – 4.4 (2.4)
Anti-PF4 by Stago ELISA	0.3 – 3.1 (1.8)	0.8 – 3.1 (1.2)	0.3 – 2.5 (1.7)
Anti-PF4 by Immucor ELISA	2.1-3.4 (2.4)	0.9 – 3.2 (2.9)	2.1-3.4 (2.7)

Table S5: Univariate and multivariate odds ratios (with 95% confidence intervals) for association between mortality and each variable in patients with VITT.

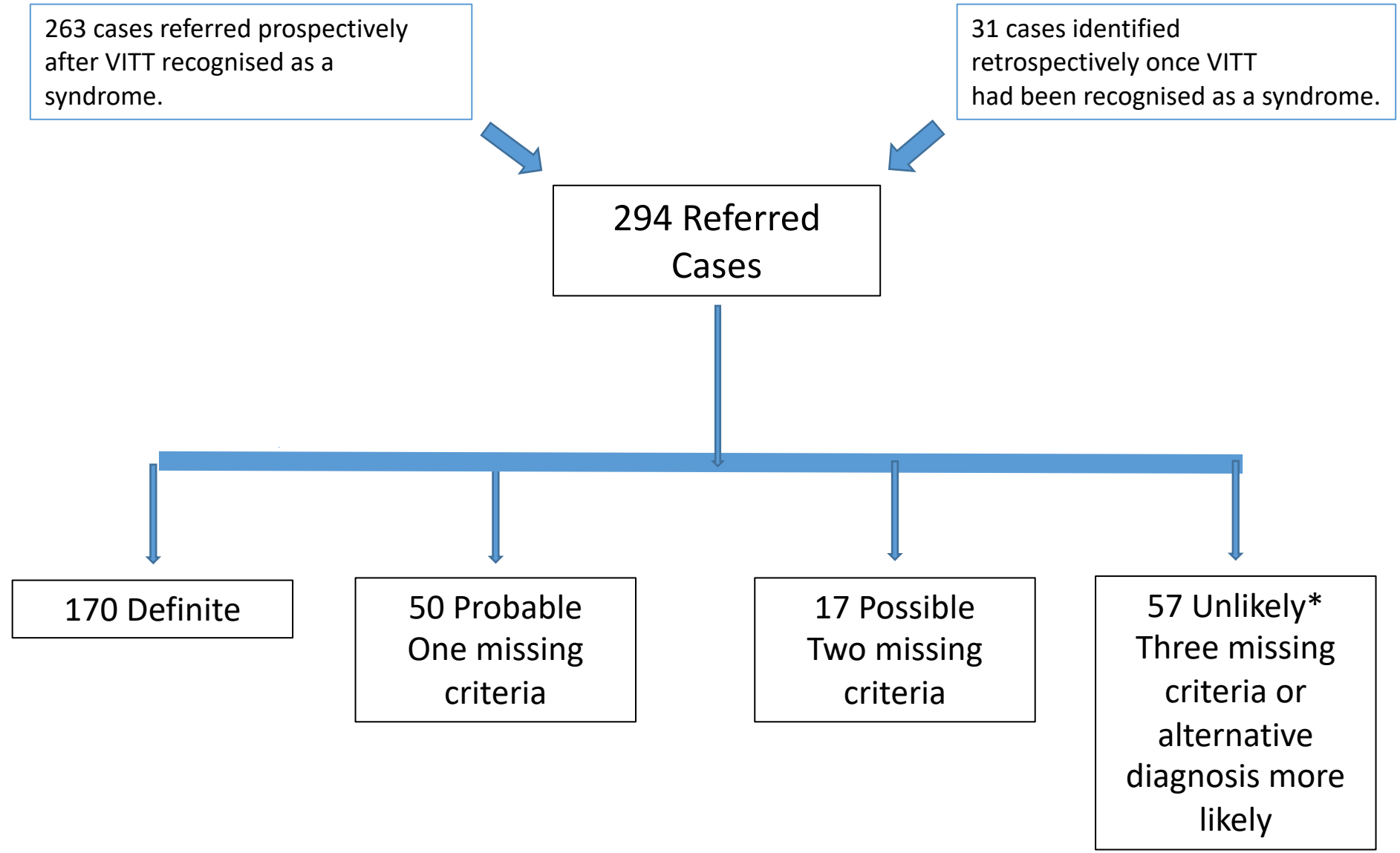
Predictor	Category	Univariate OR (95% CI)	Multivariate OR (95% CI)
Age (years)		0.991 (0.967 to 1.015)	
Sex	Male	1	
	Female	1.438 (0.745 to 2.775)	
Days from vaccine (log2)		0.704 (0.415 to 1.195)	
CVST	No	1	
	Yes	2.689 (1.386 to 5.217)	
ICH	No	1	1
	Yes	4.726 (2.335 to 9.565)	4.544 (2.188 to 9.437)
Platelet count (log2)		0.593 (0.442 to 0.795)	0.608 (0.449 to 0.822)
Fibrinogen (log2)		0.599 (0.399 to 0.899)	
D-dimer (/10000)		1.147 (1.003 to 1.312)	
PF4	Negative	1	
	Positive	0.696 (0.114 to 4.259)	

Table S6: Modalities of treatment used in patients with VITT.

Treatment modality used	Total Cohort of Definite and Probable (n=220) n (%)	Platelets <30 x 10^9/L (n=57) n (%)	Platelets ≥30 x 10^9/L (n=141) n (%)
IVIg	158 (72)	44 (77)	114 (80)
PLEX	17 (8)	9 (16)	8 (5)
Corticosteroids	58 (26)	28 (50)	30 (21)
LMWH/UFH	50 (23)	11 (19)	39 (27)
Non-heparin anticoagulation	150 (68)	34 (60)	116 (82)
Platelet transfusion	30 (14)	18 (32)	12 (9)
Interventional (Surgical or IR)	32 (15)	9 (16)	19 (13)

IVIg: Intravenous Immunoglobulin, PLEX: Plasma exchange, LMWH/UFH: Low molecular heparin or unfractionated heparin, IR: Interventional Radiology

Figure S1: Case numbers and definition of VITT in our cohort



*included 22 with insufficient data, 14 with inadequate criteria, 14 atypical presentation such as being too long after vaccine plus negative ELISA assay, or atypical features with alternative causes likely – chronic DIC from abdominal aortic aneurysm (3) and metastatic cancer (4)

Figure S2: ChAdOx1 nCov-19 vaccination and admission dates for the whole cohort by week since 1st January 2021

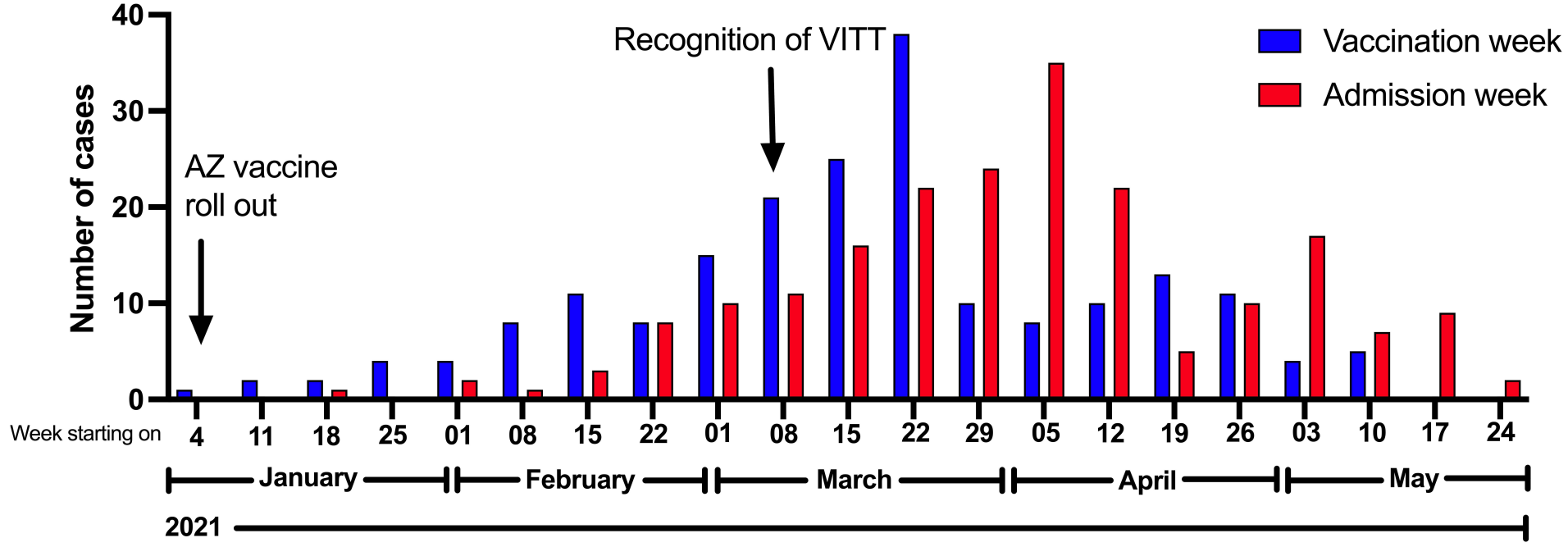


Figure S3: Sites of cerebral venous sinus thrombosis

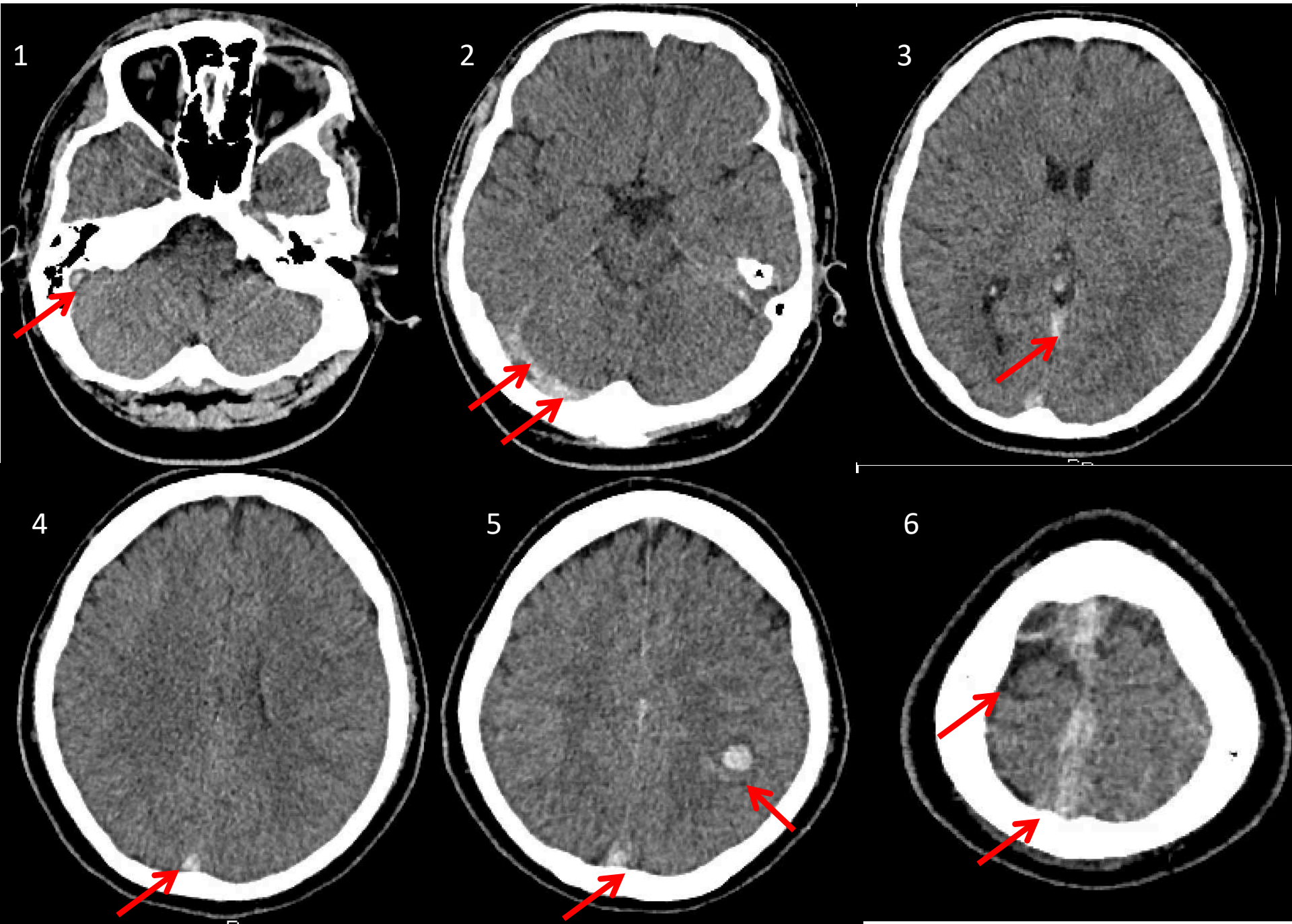
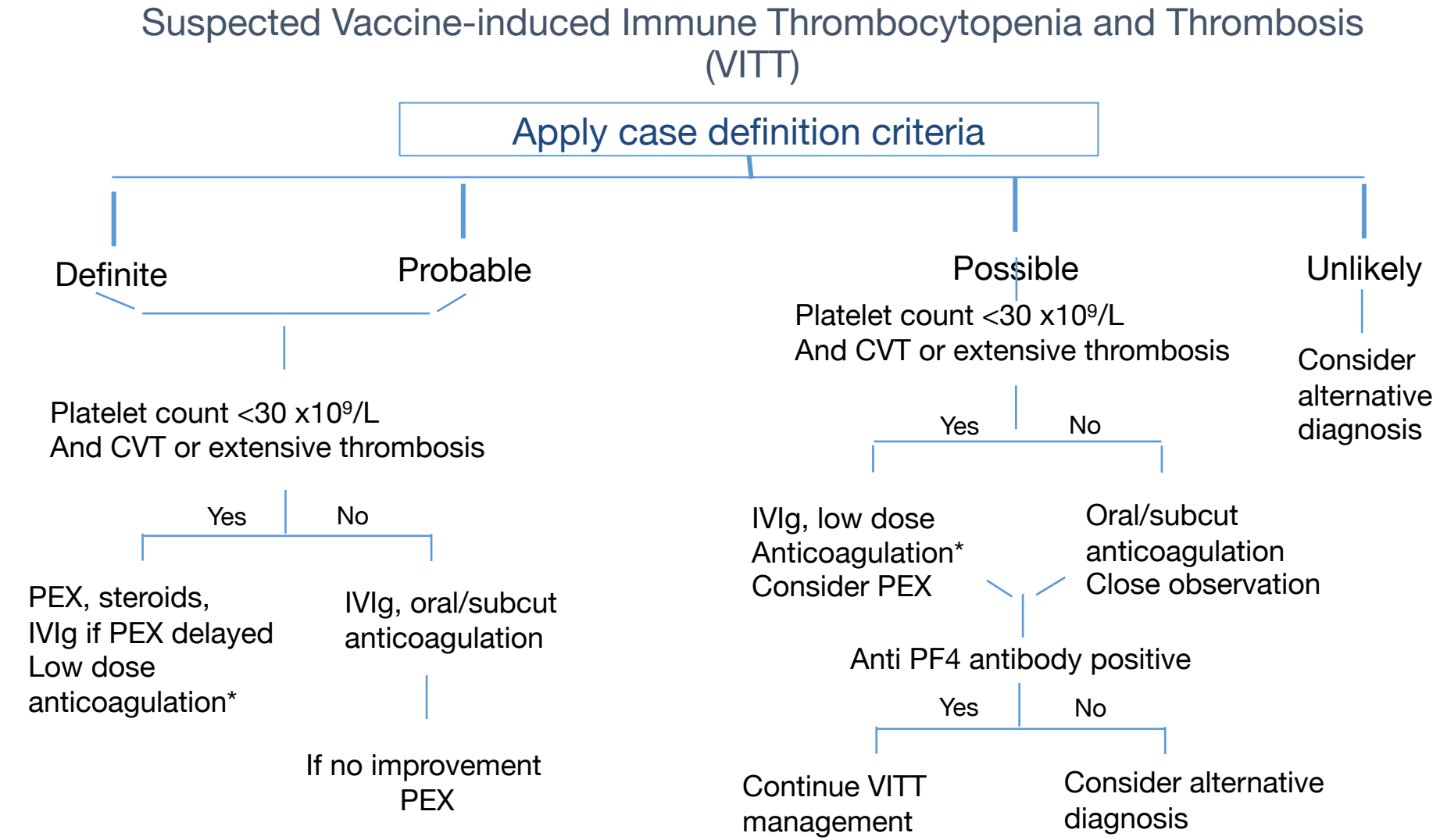


Figure S4: Revised management algorithm for patients with suspected VITT



Platelet transfusion may be required for neurosurgery, and fibrinogen supplementation if concentration <1.5g/L
Current recommendation for anticoagulation is with non-heparin-based therapies; intravenous argatroban, subcutaneous fondaparinux or direct oral anticoagulants (DOACs).
*Low dose anticoagulation is usually with critical illness dose argatroban, initiated at 0.25 to 0.5mg/kg/hr
CVT: Cerebral venous thrombosis. PEX: plasma exchange. PF4: platelet factor 4