

Supplementary Table 2: Extensive summary of case reports of BD initially presenting with psychiatric manifestations and more delayed neurological symptoms.

Citation	N ^o	Gender	Age at Diagnosis of BD (years)	Risk Factors	Psychiatric Manifestations		Neurological Manifestations		Neuroimaging Findings	Treatment
					Age of onset (years)	Symptoms	Age of onset (years)	Symptoms		
Lawrence et al (1995) (1)	1	F	58	HTN	56	Mood: Low mood (diurnal mood variations), anhedonia	57	Cognitive: Forgetfulness	CT scan: Bilateral periventricular hypodensity Mild to moderate ventricular enlargement	TCA (clomipramine) AP (trifluoperazine) ECT (6 sessions)
						Psychotic: hypochondriac delusions, intolerance of various odors, bizarre behaviors	58	Gross motor: Generalized hyperreflexia, left extensor plantar response Gait abnormalities: Stooped and dyspraxic		
	2	F	55	HTN	50	Bereavement over father's death	55	Cognitive: None reported Gross motor: Generalized hyperreflexia, increased tone in upper arms, reduced arm swing Gait abnormalities: None Others: Urinary incontinence	CT scan: Bilateral periventricular white matter hypodensity Small hypodense area in the left frontal lobe Ventricular enlargement	AP (Chlorpromazine)
54					Disorganized, bizarre behavior	55				
Summergrad and Peterson (1989) (2)	3	F	71	HTN DM HF	61	Mood: 8 years history of depression, withdrawn and being housebound Psychotic: None	69	Cognitive: memory impairment, variable attention, problems with repeated motor programs, perseveration, and stimulus	CT scan: Diffuse regions of diminished white matter attenuation in periventricular distribution	TCA (desipramine, tranylcypromine)

Citation	N ^o	Gender	Age at Diagnosis	Risk Factors	Psychiatric Manifestations	Neurological Manifestations	Neuroimaging Findings	Treatment
					Others: Poverty of speech	boundedness on trail making and clock test suggestive of frontal lobe syndrome and subcortical dementia Gross motor: None reported Gait abnormalities: Gait disturbance Others: Urinary and fecal incontinence	including the centrum semiovale	
	4	F	87	None	86 Mood: Upon admission: Fearfulness and depression; expressed a desire to die After admission: violent behavior Psychotic: Disorganized thought process Others: None reported	86 Cognitive: Impaired short-term recall, memory loss, disorientation Gross motor: None reported Gait abnormalities: None reported Others: Urinary and fecal incontinence	CT scan: Bilateral periventricular white matter hypodensity Dilated ventricles Cerebellar and cortical atrophy	TCA (tranylcypromine) AP (Haldol)

Citation	N ^o	Gender	Age at Diagnosis	Risk Factors	Psychiatric Manifestations	Neurological Manifestations	Neuroimaging Findings	Treatment	
Venna et al. (1988) (3)	5	M	68	Right cerebral infarction at 65 years old with no residual motor symptoms	65	68	<p>Cognitive: Preserved orientation and forward digit span, mild overall decline in intelligence, mild impairment in language, frontal lobe functions, recent and remote memory, striking impairment of constructional abilities</p> <p>Gross motor: Mild spastic hemiparesis, bilateral Babinski's reflex</p> <p>Gait abnormalities: None reported</p> <p>Others: Dysarthria, hypophonia, decreased upward gaze, brisk jaw reflex, masklike face</p>	<p>CT scan: Old right parietal infarction</p> <p>Bilateral low-density lesions in the periventricular white matter and centrum semiovale</p> <p>Hypodensities in centrum semiovale extended to cortical mantle</p>	MAOI (NARDIL) TCA (maprotiline)
					68				
	6	F	70	HTN	62	70	<p>Cognitive: Dementia characterized by severely impaired</p>	<p>CT scan: Bilateral white matter low</p>	TCA (imipramine)

Citation	N ^o	Gender	Age at Diagnosis	Risk Factors	Psychiatric Manifestations	Neurological Manifestations	Neuroimaging Findings	Treatment
					70 Mood: Sad, depressed, anhedonia, helplessness, hopelessness, low energy, hypersomnia, Psychotic: None Others: None reported	visual memory, significantly abnormal frontal lobe function and constructional ability on neuropsychological testing, spared language. Gross motor: None reported Gait abnormalities: None reported Others: Dysgraphia. Urinary incontinence	densities around frontal and occipital horns and the bodies of the lateral ventricles not extending to cerebral cortex	
	7	F	89	Treated: ischemic cardiomyopathy CHF DM Hypothyroidism	86 Mood: Sadness, loneliness, crying, low energy, poor appetite, early morning awakenings 89 Mood: Worsening of previous depressive symptoms Psychotic: None reported Others: None reported	89 Cognitive: Dementia with abnormalities of memory and frontal lobe function on neuropsychological testing, forward digit span and language were spared Gross motor: Bradykinesia, bilateral palmar grasp reflex Gait abnormalities: Unsteady narrow based gait Others: Occasional urinary incontinence	CT scan: Ventricular enlargement Extensive bilateral low densities limited to the perilateral ventricular regions Moderate gyral atrophy	TCA (desipramine then maprotiline)
	8	M	76	HTN CHF DM	75 Mood: Depression 76 Mood: Failure to	76 Cognitive: Confusion, on neuropsychological	CT scan: Diffuse periventricular	TCA (imipramine, desipramine)

Citation	N ^o	Gender	Age at Diagnostic	Risk Factors	Psychiatric Manifestations	Neurological Manifestations	Neuroimaging Findings	Treatment
					<p>thrive, poor appetite, weight loss, socially isolated, decreased sleep and appetite</p> <p>Psychotic: None</p> <p>Others: Apathetic</p>	<p>testing: mild overall compromise of cognitive function, dramatic deficit in visuospatial and constructional abilities, impaired visual memory, moderate loss of set shifting.</p> <p>Preserved orientation, forward digit span, verbal fluency language production</p> <p>Gross motor: Bradykinesia, paratonic rigidity of all limbs,</p> <p>Gait abnormalities: Slow</p> <p>Others: Dysgraphia, occasional urinary incontinence</p>	<p>low densities that did not involve centrum semiovale and did not extend to the cortex.</p>	
Nages and Nujan Nagaratnam (1998) (4)	9	F	88	HTN	<p>Mood: agitation; aggression</p> <p>Psychotic: Late-onset paranoid delusions with religious overtones, thought process loosely associated</p>	<p>88</p> <p>Cognitive: Memory normal for age</p> <p>Gross motor: Left extensor plantar response at presentation. Subsequently developed swallowing difficulties from pharyngeal incoordination</p>	<p>CT scan: Extensive white matter changes in relation to ventricles</p> <p>Small focal densities in the regions of basal ganglia (lacunar infarctions)</p>	-

Citation	N ^o	Gender	Age at Diagnostic	Risk Factors	Psychiatric Manifestations	Neurological Manifestations	Neuroimaging Findings	Treatment
							Gait abnormalities: None reported	
	10	F	77	None	77 Mood: agitation; aggression Psychotic: Persecutory delusions, auditory hallucinations Others: None reported	77 Cognitive: Confusion, reduced attention span Gross motor: None reported Gait Abnormalities: None reported	CT scan: White matter low attenuation in relation to frontal horns and borders of lateral ventricles Widening of Sylvian fissures Widened cortical sulci Widening of ventricular system	-
	11	M	70	HTN Smoker Short systolic murmur in aortic area Left CVA at age 67	70 Mood: Emotionally labile, quick to anger, socially withdrawn, anhedonia, loss of functionality Psychotic: None reported Others: None reported	71 Cognitive: Significant intellectual deterioration Gross motor: None reported Gait abnormalities: Abnormal gait since CVA Other: Significant functional impairment	CT scan: Severe white matter low attenuation in relation to ventricles Small hypodense area in the left internal capsular area Lacunar infarction lateral to the right frontal horn	-

Citation	N ^o	Gender	Age at Diagnosis	Risk Factors	Psychiatric Manifestations	Neurological Manifestations	Neuroimaging Findings	Treatment
	12	M	65	DM CAD CHF Stroke	- Mood: None reported Psychotic: None reported Others: Behavioral disturbances of frontal lobe type	- Cognitive: Intact Gross motor: Stiffness and clumsiness of right hand Difficulty walking but no weakness Bilateral slow dysrhythmic finger movement of both hands Gait abnormalities: None reported	CT scan: White matter changes that do not extend to cortex Hypodense areas of ill-defined borders in frontal lobes of both hemispheres	-
Pathania et al (2018) (5)	13	F	55	uncontrolled HTN DM DL	- Mood: Depressed mood Psychotic: None reported Others: Behavioral disturbances of frontal lobe type	52 Cognitive: Forgetfulness, lack of concentration, decreased attention span Gross motor: Problems in articulation, intentional tremor, abnormal coordination Gait abnormalities: unsteady gait Others: Impairment in ADL (eating, bathing)	MRI: Hemorrhagic infarct in the right thalamus with extensive chronic ischemic white matter lesions	Cholinesterase inhibitor

Citation	N ^o	Gender	Age at Diagnosis	Risk Factors	Psychiatric Manifestations	Neurological Manifestations	Neuroimaging Findings	Treatment		
El Shazly 1994 (6)	14	F	62	HTN	59	Mood: Depressed agitated mood, suicidal ideations, poor concentration, poverty of speech, worthlessness, hopelessness followed by a hypomanic state while on trimipramine	62	Cognitive: Fluctuating level of conscious awareness, short term memory deficits, marked constructional deficits on neuropsychological tests Gross motor: Generalized hyperreflexia, tremor, oral dyskinesia Gait abnormalities: Tottering gait Others: None reported	CT scan with contrast: Well-marked multiple areas of loss of attenuation in white matter seen in both hemisphere consistent with lacunar infarcts	TCA (trimipramine, amitriptyline) SSRI (fluvoxamine) AP (amoxapine, Haldol) Lithium, carbamazepine ECT (3 courses)
					59 – 61	Mood: Rapid cycling bipolar illness where depressive and hypomanic episodes alternates and were resistant to treatment with antidepressants, ECT and mood stabilizer				
					62	Mood: Less severe mood cycling predominantly labile with generalized anxiety Psychotic: None reported Others: None reported				

References:

1. Lawrence R, Hillam J: Psychiatric symptomatology in early-onset Binswanger's disease: two case reports. *Behavioural neurology* 8:43-6, 1995
2. Summergrad P, Peterson B: Binswanger's disease (Part I): the clinical recognition of subcortical arteriosclerotic encephalopathy in elderly neuropsychiatric patients. *Topics in geriatrics* 2:123-33, 1989
3. Venna N, Mogocsi S, Jay M, et al.: Reversible depression in Binswanger's disease. *The Journal of clinical psychiatry* 49:23-6, 1988
4. Nagaratnam N, Nagaratnam K: Psychiatric and behavioral aspects of dementia of the Binswanger type. *American Journal of Alzheimer's Disease* 13:173-8, 1998
5. Pathania M, Amisha PM, Rathaur VK, et al.: A case of hypertension with dementia: Common but underdiagnosed. *Journal of family medicine and primary care* 7:447, 2018
6. El-Shazly M: Rapid cycling bipolar disorder in a case of Binswanger's disease. *International Journal of Geriatric Psychiatry* 9:925-7, 1994