Aggressive evaluation, management and monitoring of MCI/dementia syndromes

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Of approximately 1770 patients over the age of 50 years old referred to the Falls Memory Center from 2007-present, approximately 1020 or 58% have And the second s or dementia

Aggressive evaluation and management includes genetic testing for MTHFR, A1AT polymorphisms and in suitable cases APOE genetic testing. Significant comorbidities include vasculopathic MTHFR polymorphisms (58%), B12 deficiency (25%), and obstructive sleep apnea (24% of patients). Management includes genetic counseling, directed vitamin supplementation (B12, folate/riboflavin), treatment of sleep disorders, and usual medications such as acetylcholinesterase inhibitors, memantine and antidepressants/anxiolytics.

In addition to bedside psychometric screens, selected patients received a computerized cognitive battery (CNS Vital Signs) for staging and monitoring Often given at intake and first revisit (baselining), the test takes 30-40 minutes and allows greater definition of deficits particularly for persons with MC syndromes with MMSE>23

Control of the multiple factors affecting behavior and cognition in patients with MCI/dementia syndromes can produce stabilization or improvement in many cases. Monitoring clinical course with computer testing can facilitate assessment and provide a basis for patient and family instruction/compliance with the treatment regimens. Improvement is particularly common with targeted therapy of the vasculopathic MTHFR alleles; examples will be shown.

Most neurodegenerative syndromes are multifactorial, genetic/environmental illnesses. Effective intervention is possible through identifying and treating all complicating factors. [Support by Guardian Angel Thrift Foundation, KB Reynolds Foundation, Duke Endowment]

Disease Mode

The caricature is "single pure entities" with response to single pharmacological interventions. Multiple factors result in heterogeneity and variance eve In clathed is any port ended with response to single phatmackedge interventions, including tack are set in the original water and the set in relatively "pure" genetic cases since these illnesses represent the result of complex environmental and genetic factors further complicated by different responses of patient and caregiver with regard to treatment, compliance and behavioral modulation. We will offer evidence that most cases are in fact multifactorial, most commonly mixed etiology dementias with AD and vascular component. As aggressive evaluation and management is initiated, the key issues are tracking the clinical trajectory of patients and continuing to address both primary and secondary factors

Practice Model

The model was based on team approach with physician, physician extender (physician associate), medical social worker (currently an RN with home The theorem as dealed of them tagk but with representation of the providence in the providence in the tagk but with the tagk but with the providence in the tagk but with the tagk but with the tagk but with the tagk but with tagk b

Medical D

OPSG

Initial D

Final Dx

Medical Dx

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Summary: 63 year old man presenting with significant memory

and concentration problems in MCI range, onset age 60. Intact ADL and IADL, but disabling problems in job performance and memory. Work-up reveals OSA/UARS and "normal" MTHFR alleles C677T/wt, also AITD, B12 deficiency. Given wm disease, (-

) work-up for MS. Treatment goals: biPAP treatment, omega-3

vears with stability. CNS VS allowed fine characterization of

steps: omit biPAP to see if difference w/r sleep efficiency...

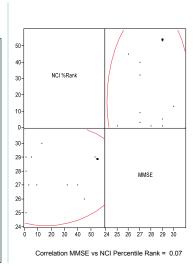
clinical course, including recent decline in performance. Patient and wife positively influenced by revelation of testing performance

- useful in demonstrating current status since MMSE stable. Next

supplementation, exercise, treatment of AITD. Follow-up over 1.5

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СІ		First Visit	Second Visit 4-6 weeks	2 month Visit	2-6 month depending on Intervention	
	History and Physical					50
	Neurocognitive Exam •					40
ng. ICI	Cognitive Screening	•				30
n	Social work consultation and overview	•				20
	Review/order neuroimaging, sleep studies etc	-•				10
	Blood work •	•				0
	Genetic Testing	•				30
/en	Other Blood Work (homocysteine, inflammatory indices etc)					29
;	Establish primary, secondary, medical diagnoses	•				28
	Computerized testing (CNS Vital Signs)	•				27
e	Review of Clinical Status •				— •	26 25
	Review of genetics, blood work, imaging		•			23
а	Revision of Diagnoses		•			
	Selection of interventions, nutifional, pharmacologic, exercise •—	-		•		



Summary

1) Most cases of MCI/dementia have multiple factors, particularly vascular

2) Factors that can be identified include sleep disorders, vasculopathic factors including diabetes, dyslipidemias, MTHFR alleles (homocysteine metabolism), nutritional

3) Aggressive evaluation will often include genetic testing to help in differential diagnosis and treatment selection

4) Treatment will then involve multiple therapies and interventions

5) Staging and monitoring can be assisted by cognitive testing at relatively frequent intervals, including short screens such as MMSE of MOCA forms.

6) Finer detail ("granularity") can be revealed using computer cognitively testing such as here illustrated by CNS Vital Signs battery Test can be administered by support personnel, takes 30-40 minutes and has alternate forms. Most patients with high school education and reasonable exposure to computers can handle testing. Familiarity and practice effects can be dealt with by leading in with two baselines prior to monitoring.

MCI and dementia are treatable disorders, involving complex interactions of genes-environment including behavioral responses and life practices of patient and caregiver.

8) Clinical stability and improvement should be sought for assiduously by dealing with all reasonable treatable factors impacting behavior and cognition

Summary: 60 year old man presenting with significant memory	MMSE 25	MMSE 29	MMSE N/A	MMSE 26	MMSE 27	MMSE 27
 Summary and convertation problems in MC range, onset age 57. Intact and convertation problems in MC range, onset age 57. Intact ADL and IADL but disbling problems in Job performance. Work- uples 69. The Convertation of the Convertation of the Convert and the Convertation of the Convertation of the Convert and the Convertation of the Convertation of the Convert and the Convertation of the Convertation of the Convertation of the Convertation of the Convertation of the Convertation remained inspared, but attention of the Convertation remained inspared, but attention and memory domains also responding, possibly more related to CPAP compliance. Pattent and wife positive further of the Convertation of testing performance - useful in demonstrating probable effects of compliance. Pattent and wife positive further one APCE and consideration of additonal therapies: AChEI, memantine, axona. 						

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	White female presenting at age 68 with memory problems
MRI	Moderate subcortical vascular disease
OPSG	PLMS
Genetics	APOE 3/4 MTHFR gene C677T/A1298C compound heterozygote
Initial Dx	Non amnestic MCI
Final Dx	Early AD with vascular components
Secondary Dx	PLMS
Medical Dx	Possible nutritional compromise Ethanol Dyslipidemia
Therapy	PLMS treatment Taper and D/C alcohol
Meds	Metfolate/riboflavin for MTHFR Simvastatin Gabapentin 600 hs for PLMS Omega-3 2000 mg gd

SAUARS

Early AD with va

B12 deficient autoimmune thyroid dis

BIPAP for OSA/UARS

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wothyroxine suppret mega-3 2000 mg qd

on of AITD

mantine wastatin

APOE 4/4 MTHFR gene C677T/wt

THFR gene C677T/C677

Omega 3 2000 mg qd

White female presenting at age 68 with memory problems	Summary: 68 year old woman presenting with significant memory and concentration problems in MCI range, onset age 65. Intact ADL and IADL, but intermittent problems in memory
Moderate subcortical vascular disease	and concentration noted by friends and family. Work-up reveals PLMS and vasculopathic MTHFR alleles
PLMS	C677TA1298C. Treatment goals: PLMS treatment, omega-3
APOE 3/4 MTHFR gene C677T/A1298C compound heterozygote	supplementation, exercise, treatment of MTHFR alleles. Follow-up over 2.25 years with stability/improved MMSE. CNS VS allowed fine characterization of clinical course. including improvements in
Non amnestic MCI	performance. Patient and husband positively influenced by
Early AD with vascular components	revelation of testing performance - useful in demonstrating current
PLMS	status since MMSE relatively stable. Next steps: emphasis of
Possible nutritional compromise Ethanol Dyslipidemia	nutritional factors.
PLMS treatment Taper and D/C alcohol	
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Clinical experience at Falls Neurology and Memory Center

Patient population:

2584 total consecutive natients since 7/2007 to date

-1770 patients over age of 50 years -1023 or 57.8% disorders of memory or concentration or neurodegenerative disor

Distribution of diagnoses: -Mild syndromes: CIND 0.9%, adult ADD 1.4%,

-MCI / AD syndromes: aMCI 18.6%, AD 4.1%, ADVD 14.7%, ADPD 2.3%, LBD 0.5% -Non-AD syndromes: naMCI 7.8%, FTD/FTDPD 4.5%, PD 5.8%, PPA 4.2%, PSP 0.3%, VD 1.5%

Gender distribution: 61% female Average follow-up: 2.0 years

Complicating secondary medical or anatomical diagnoses all patients

-Obstructive sleep apnea - 24.3% -PLMS/RLS - 7.0% -REM-BD - 2.3%

-Adult onset diabetes - 25 7%

-Coronary artery disease (Afib, CABG, stenting,...) – 22.3% -B12 deficiency - 18.7% new, 6.8% additional cases previously treated

White matter abnormalities - ca 70% of cases

Genetic testing

A1AT: PIMM 84.5%, PIMS 9.5%, PIMZ 3.6%, PIFM 1.3%, other 1.1% (n=1756) MTHFR: wt or single mutation- 58.6%, C677Tx2 12%, A1298Cx 2 8.4%, C677T/A1298C 21% (n=1725) C282Y C282Y/+ 13 3% +/+ 86 8% C282Y/C282Y 0 9% (n=659) APOE: E44 13.4%, E34 42.7%, E33 34.6%, E24 1.7%, E23 7.7% (n=239)

[A1AT = alpha1-antitrypsin; MTHFR = methylene tetrahydrofolate reductase; C282Y = locus for hemochromatosis mutation; APOE = apolipoprotein E]

Contact

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