Pediatric Grand Rounds
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Financial Disclosure
The presenters, discussants and I have no financial relationships to disclose.
Megalencephaly-Capillary Malformation Polymicrogyria (M-CAP):
A Case Study

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Objectives

• M-CAP
  – Diagnostic Criteria
  – Identifiable Characteristics
  – Literature
  – Treatment

• Case Study
  – Demographics
  – History
  – Evaluation Results
  – Recommendations
Demographics

- Rare syndrome first described in 1997
  - Multiple name changes given defining characteristics (M-CMTC, M-CM, M-CAP)
  - In 2012, Genetic mutation identified in gene PIK3CA
  - Mutation is thought to always occur after cell division begins - de novo mutation

- Website Registry = 181 cases

<table>
<thead>
<tr>
<th>Age</th>
<th># Registered</th>
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<tbody>
<tr>
<td>0-2 yrs</td>
<td>32</td>
</tr>
<tr>
<td>3-10 yrs</td>
<td>100</td>
</tr>
<tr>
<td>11-18 yrs</td>
<td>37</td>
</tr>
<tr>
<td>18+ yrs</td>
<td>12</td>
</tr>
</tbody>
</table>

- Literature Reports = 150 cases
- Across genders
- Across ethnicities

http://works-progress.com/portfolio/m-cm-network/

Diagnostic Criteria

- Proposed Clinical Criteria for Diagnosis (Martínez-Glez et al., 2010)

<table>
<thead>
<tr>
<th>Major Criteria (requires 3)</th>
<th>Minor Criteria (requires 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrocephaly *</td>
<td>Midline facial capillary malformation</td>
</tr>
<tr>
<td>Capillary malformation(s) *</td>
<td>Neonatal hypotonia</td>
</tr>
<tr>
<td>Overgrowth/asymmetry *</td>
<td>Syndactyly/polydactyly *</td>
</tr>
<tr>
<td>Neuroimaging alterations:</td>
<td>Connective tissue abnormalities</td>
</tr>
<tr>
<td>o Ventriculomegaly *</td>
<td>Frontal bossing</td>
</tr>
<tr>
<td>o Cavum septum pellucidum or cavum septum vergae</td>
<td>Hydrocephalus *</td>
</tr>
<tr>
<td>o Cerebellar tonsillar herniation</td>
<td>Developmental delay *</td>
</tr>
<tr>
<td>o Cerebral and/or cerebellar asymmetry *</td>
<td></td>
</tr>
</tbody>
</table>

Martínez-Glez et al. were able to diagnose 94% of 136 previously reported cases using their criteria.
Identifiable Characteristics

- **Macrocephaly**
  
  http://undiagnosed.org.uk/archives/tag/macrocephaly
  
  http://www.m-cm.net/

- **Capillary Malformation(s)**
  

- **Overgrowth / Asymmetry**
  
  https://www.edmcasereports.com/
  
  http://www.m-cm.net

- **Neonatal Hypotonia**
  
  http://autism.wikia.com/wiki/Hypotonia

- **Syndactyly / Polydactyly**
  
  http://www.m-cm.net
  
  http://www.wikipedia.org

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Literature

- Limited cognitive / neuropsychological data

- Most studies suggest developmental delays ranging from mild to moderate impairment

- For example: Mirzaa et al. (2012) examined 21 MCAP children

  100% Developmental Delay

  38% Profound Language Delay  n = 8

  28% Autistic Symptoms  n = 6

  5% ADHD  n = 1

  5% ADHD / OCD  n = 1

  5% Normal Intelligence  n = 1
Important Note:
- To date, MCAP does not appear to be a condition associated with regression or decline in a person's cognitive functioning; unless an exacerbation of neuropathological processes occurs.
- Children with MCAP are expected to make slow progress developmentally.
- However, most children with this disorder continue to be consistently behind their peers in both academic and functional abilities.

CHALLENGE
This diverse presentation proves to be an obstacle when trying to identify cognitive or behavioral patterns in MCAP.

Currently, there is no cure for M-CAP

Treatment varies depending on a multitude of factors including the presence and severity of specific impairments.
CASE STUDY

• Frances “Franny” Brown
• Diagnosed with M-CAP at age 4 months
• Referral
  – Global delays
  – Reported inattention
  – Recent academic deficits / regression

<table>
<thead>
<tr>
<th>Gender</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>7</td>
</tr>
<tr>
<td>Education</td>
<td>1st grade public education</td>
</tr>
<tr>
<td>Handedness</td>
<td>Right</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Caucasian</td>
</tr>
<tr>
<td>Socioeconomic Status</td>
<td>Upper Middle Class</td>
</tr>
<tr>
<td>Parental Education</td>
<td>Bachelors Degree</td>
</tr>
</tbody>
</table>

Developmental History

• Prenatal history uncomplicated
• Upon delivery, presented with
  – Cutis marmorata
  – Port wine stains
  – Large head (95th percentile – then “off the chart”)
  – Feet malformations
• Genetic testing - none
• All developmental milestones delayed
• Continued motor deficits
Medical History

- **Macrocephaly**
- **Hemihyperplasia**
- **Capillary malformations**
- Headaches
- **Hydrocephalus**
  - Partial complex seizures (age 2 ½)
- **Syndactyly / polydactyly**
  - Muscle spasms
  - Bladder incontinence
  - Chronic ear infections
  - Comorbid hearing impairment
  - Currently wears hearing aids in both ears

- **Surgery History (to date):**
  - Ventriculoperitoneal shunt
    - (2 revisions)
  - Fourth ventricle shunt
    - (1 revision)
  - Tonsillectomy
  - Adenoidectomy
  - Spinal fenestration of an arachnoid cyst
  - Chiari decompressions (3)
  - Spinal shunt
    - (1 revision)

- **Medications**
  - Keppra, Trileptal, prevacid

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Medical History

- **Neuroimaging (MRI) Findings:**
  - Brain asymmetry / left hemimegalencephaly
  - Hydrocephalus (shunt placements)
  - Chiari malformations
  - Distortion of cerebellar hemisphere
  - White matter signal hyperintensities
Previous Evaluation

2012

Test Results:
Intelligence / Achievement / Memory

WISC-IV        WIAT-III       LEITER-R

Standard Score

Gf: 57 69 70 55 59 60 60 65 51 76 105 110
Vocabulary: 66 70 60 60 65 51 76 105 110
Similarities: 55 59 60 60 65 51 76 105 110
Comprehension: 55 59 60 60 65 51 76 105 110
Per: 55 59 60 60 65 51 76 105 110
Block Design: 55 59 60 60 65 51 76 105 110
Matrix Reasoning: 55 59 60 60 65 51 76 105 110
Picture Concepts: 55 59 60 60 65 51 76 105 110
Digit Span: 55 59 60 60 65 51 76 105 110
Early Reading Skills: 55 59 60 60 65 51 76 105 110
Receptive Vocabulary: 55 59 60 60 65 51 76 105 110
Immed. Visual Memory: 55 59 60 60 65 51 76 105 110
Daily Visual Memory: 55 59 60 60 65 51 76 105 110

CTOM 73 76 90 82 50
WJ-III 73 76 90 82 50
Letter-Word Identification 73 76 90 82 50
Passage Comprehension 73 76 90 82 50
Arithmetic Problems 73 76 90 82 50
Writing Sample 73 76 90 82 50
Test Results: Adaptive Functioning

<table>
<thead>
<tr>
<th>Domain</th>
<th>Age Equivalent</th>
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</thead>
<tbody>
<tr>
<td>Communication</td>
<td></td>
</tr>
<tr>
<td>Receptive</td>
<td>1:10</td>
</tr>
<tr>
<td>Expressive</td>
<td>2:6</td>
</tr>
<tr>
<td>Written</td>
<td>3:1</td>
</tr>
<tr>
<td>Daily Living</td>
<td></td>
</tr>
<tr>
<td>Personal</td>
<td>2:9</td>
</tr>
<tr>
<td>Domestic</td>
<td>2:8</td>
</tr>
<tr>
<td>Community</td>
<td>3:7</td>
</tr>
<tr>
<td>Socialization</td>
<td></td>
</tr>
<tr>
<td>Interpersonal</td>
<td>2:3</td>
</tr>
<tr>
<td>Play and Leisure</td>
<td>2:11</td>
</tr>
<tr>
<td>Coping</td>
<td>2:11</td>
</tr>
</tbody>
</table>

Vineland Adaptive Skills – 2nd Edition

Test Results: Executive Functioning

<table>
<thead>
<tr>
<th>Domain</th>
<th>T-Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibit</td>
<td>58</td>
</tr>
<tr>
<td>Shift</td>
<td>61</td>
</tr>
<tr>
<td>Emotional Control</td>
<td>66</td>
</tr>
<tr>
<td>Initiate</td>
<td>62</td>
</tr>
<tr>
<td>Working Memory</td>
<td>65</td>
</tr>
<tr>
<td>Plan / Organize</td>
<td>73</td>
</tr>
<tr>
<td>Org of Materials</td>
<td>55</td>
</tr>
<tr>
<td>Monitor</td>
<td>58</td>
</tr>
</tbody>
</table>

Behavior Rating Inventory of Executive Function
Test Results:
Behavior and Emotional Screening

<table>
<thead>
<tr>
<th>Behavior</th>
<th>T-Score</th>
<th>Interpretation / Take Home</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperactivity</td>
<td>47</td>
<td>Consistent with MCAP literature, Franny presented with multiple neurologic complications which should raise concerns and can impact cognitive development</td>
</tr>
<tr>
<td>Aggression</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Conduct Problems</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td>Somatization</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>Appetite</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Withdrawal</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Attention</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td>Learning Problems</td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>School Problems</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>Single Word Reading</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Written Expression</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>Motor Problem</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Social Problems</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Reading Comprehension</td>
<td>70</td>
<td>Most concerning was that cognitive performance had declined NOT TYPICAL</td>
</tr>
<tr>
<td>Language Comprehension</td>
<td>63</td>
<td></td>
</tr>
</tbody>
</table>

Comorbid hearing impairment made for additional challenges
Recommendations

• Educational Placement
  – Individualized Education Plan (IEP)
  – Hearing impaired specialist for teacher
  – Instruction should take place in a 1-on-1
  – Integration into general education
  – Speech and Language Therapy, Occupational Therapy, and Physical Therapy

• Neurology Consultation
  – Urgent given regression

• Cognitive and Academic Recommendations:
  – Implement visual instruction / learning
  – Make learning meaningful
  – Focus on functionality
  – Repetition is key
  – Provide a structured and explicit learning environment
  – Attention
  – Reading
  – Rewards plan

• Neuropsychological Re-Evaluation.
  – Annually

References

Questions and Discussion

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Neuropsychological Profile of Pediatric Pseudotumor Cerebri Syndrome: A Case Study

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¹University of Tennessee Health Science Center,
²The University of Kansas Medical School- Wichita
Introduction

• Pseudotumor cerebri syndrome (PCS) is a progressive disorder marked by increased intracranial pressure without a known cause.
• A rare disorder in children, particularly prior to the age of 11
• Research on PCS related cognitive deficits have almost exclusively investigated adults.
• This presentation will provide a case study of childhood PCS

Pseudotumor Cerebri Syndrome (PCS)

Symptoms
• Mimics sx of brain tumor
• Headache
• Papilledema
• Blurred vision
• Increased CSF pressure

Course
• Develops over weeks or months
• Absence of enlarged ventricles or a mass
• Most common in obese adult women of childbearing age

Treatment
• Lumbar-peritoneal shunting
• Lumbar puncture
• Corticosteroids
• Weight reduction
Previous Literature

- Limited research into cognitive implications of PCS
  - Adult studies ranging from 20y – 56y, with one 15yo included
  - Almost exclusively female

- Most common findings
  - General verbal deficits in language, memory, and fluency
  - General memory deficits
  - Executive dysfunction and poor cognitive flexibility
  - Slowed processing speed and reaction time
  - Visual-spatial deficits

- Most patients do not show cognitive improvement, despite treatment

- No patients show evidence of brain damage/malformation on CT/MRI to indicate cause of impairment

Case study: 12-year-old female “K”

Reason for Referral
- Memory difficulties
- Academic difficulties
- Impaired sense of time
- Impaired hygiene
- Fatigue and poor sleep

Demographics
- 6th grade with 504 plan
- Right-handed
- PCS diagnosed in 2011 (9yo)
  - Papilledema
  - Daily headaches
- BMI – 97th percentile

Developmental history
- Unremarkable pregnancy/birth
- Milestones achieved within normal limits
- Medical history unremarkable

Current medical issues
- Optic Nerve Drusen w/papilledema
- 1-2 headaches per month
- Snoring and daytime sleepiness
- No prescribed medications
- Unremarkable MRI/MRV (repeat studies)

Surgical history
- Strabismus 2013, 2014
- Lumbar peritoneal shunt 2013
# Tests Administered

<table>
<thead>
<tr>
<th>Domain</th>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intelligence</td>
<td>Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV)</td>
</tr>
<tr>
<td>Academic Achievement</td>
<td>Woodcock-Johnson Tests of Achievement, Third Edition (WJ-III)</td>
</tr>
<tr>
<td></td>
<td>Gray Oral Reading Tests, Fifth Edition (GORT-5)</td>
</tr>
<tr>
<td>Language</td>
<td>Boston Naming Test</td>
</tr>
<tr>
<td></td>
<td>Peabody Picture Vocabulary Test, Fourth Edition (PPVT-4)</td>
</tr>
<tr>
<td></td>
<td>Expressive Vocabulary Test, Second Edition (EVT-2)</td>
</tr>
<tr>
<td>Motor</td>
<td>Grooved Pegboard Test</td>
</tr>
<tr>
<td>Visuoperceptual</td>
<td>Benton Judgment of Line Orientation (JLO)</td>
</tr>
<tr>
<td></td>
<td>Beery Developmental Test of Visual Perception</td>
</tr>
<tr>
<td></td>
<td>Beery Developmental Test of Visual-Motor Integration (VMI)</td>
</tr>
<tr>
<td>Memory</td>
<td>Test of Memory and Learning, Second Edition (TOMAL-2)</td>
</tr>
<tr>
<td></td>
<td>Rey-Osterrieth Complex Figure Test (RCFT)</td>
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<tr>
<td>Executive Functioning</td>
<td>Delis-Kaplan Executive Function System (D-KEFS)</td>
</tr>
<tr>
<td></td>
<td>Wisconsin Card Sorting Test (WCST)</td>
</tr>
<tr>
<td>functioning</td>
<td>Behavior Rating Inventory of Executive Function (BRIEF)</td>
</tr>
<tr>
<td></td>
<td>Behavior Assessment System for Children, Second Edition (BASC-2)</td>
</tr>
</tbody>
</table>

## Results: Intelligence

![WISC-IV Results Chart](chart.png)
Results: Academic Achievement

- Calculation: 94
- Math Fluency: 90
- Applied Problems: 70
- Spelling: 85
- Letter-Word: 80
- Oral Reading Index: 85

Results: Language

- BNT: 50
- PPVT-4: 80
- EVT-2: 88
Results: Visuospatial and Motor

- Benton JLO: 64
- Berry Visual Perception: 85
- Berry VMI: 72
- Pegboard Dom Hand: 76
- Pegboard Non-Dom Hand: 53

Results: Memory

- Memory for: 75
- Story Delayed: 55
- Word: 75
- Word: 70
- Facial Memory: 100
- Abstract: 70
- RCT: 70
- RCT Delayed: 70
- RCT: 96
Results: Executive Functioning

Impressions

- Overall borderline impaired intellectual functioning and mildly impaired adaptive functioning
- Diffuse impairment in multiple areas of functioning
  - Comprehension
  - Memory across domains
  - Visual-perception and visual-construction
  - Motor speed/coordination
  - Confrontational visual naming/word retrieval
- Pockets of preserved cognition
Treatment Recommendations

• Changes to modifications/accommodations on implementation of IEP
• Strategies for slow learners emphasizing dividing tasks in to smaller units, repetition with frequent practice
• Use of visual memory aids and routines to maintain consistency
• Mathematics tutoring and reading comprehension intervention
• Chart system for hygiene
• Referral to the Sleep Disorders Clinic

Case in Context

• In comparison to previous literature
  • Pattern of deficits were largely consistent with previous literature.
  • Particularly notable is her Borderline IQ with greater deficits in Verbal Comprehension – many adults did not have general impairments in IQ
• Relevance to field
  • Although some view PCS as a “benign” condition, our findings suggest that diffuse cognitive deficits and impaired functioning are likely and will require intervention
  • Will the condition become more prevalent in children as childhood obesity rises?
Questions

References


The Need for Collaboration

- Pediatric neuroimmunology is a rapidly changing field with many unknowns.
- Functional neurological symptoms are also poorly understood in children, and often considered only when medical causes are ruled out.
- This case highlights the need for collaboration between neuropsychologists and neurologists.
Demographics and Reason for Referral

- Kate: 12 year old Caucasian girl with suspected autoimmune encephalitis
- Normal early history until onset of symptoms two years ago
- Withdrew from rigorous private school in order to homeschool
- Participation in competitive gymnastics league
- Only child, living with both parents
- Family history noncontributory

Symptoms

- “Disney Princess” voice and mannerisms appeared following strep throat infection
- Approximately six months later developed additional neurological symptoms following urinary tract infection and flu mist vaccine
  - Dilated pupils
  - Agitation
  - Repetitive and tic-like behaviors
  - Dizziness
  - Headaches
  - Cognitive changes (memory, math, “brain fog”)
  - Slurred/pressured speech
  - “Emotional fatigue”
- Symptoms worsened and she was “almost comatose”
Medical Evaluations and Testing

- Multiple previous specialists
  - Neurology
  - Gastroenterology
  - Psychiatry
  - Infectious Disease
  - Chiropractic
  - Applied Behavior Analysis
  - Complementary and Alternative Medicine

- Negative strep titres
- Normal MRI of the brain
- Normal EEG

- Abnormal CSF results
  - Elevated interleukin 6 and 8
  - S100B of unclear significance

Treatments

- Injection of rocephin (symptom improvement for 24 hours)
- Intravenous immunoglobulin (brief improvement)
- Plasmapheresis (brief improvement)
- Scheduled to undergo additional intravenous immunoglobulin treatments
Initial Testing: Selected Scores

Performance on all tests represented as standard scores with higher scores reflecting optimal performance.

Initial Testing: Parent Rating Selected Scores

Performance on all tests represented as standard scores with higher scores reflecting optimal performance.

Performance on all tests represented as standard scores with higher scores reflecting optimal performance.

Impressions and Recommendations

- Autoimmune encephalitis
  - Continue with plan for intravenous immunoglobulin
  - Neuropsychological re-evaluation post-treatment
- Functional neurological symptoms
  - Consider psychotherapy for stress management and coping skills
Two Months Later

- Additional course of intravenous immunoglobulin completed
- No other treatments or changes
- Family reports improvements in symptoms
  - Memory problems and “brain fog”
  - Voice and mannerisms
  - Anxiety
- Improvements most noticeable immediately following treatment

Follow-Up Testing: Selected Scores

Performance on all tests represented as standard scores with higher scores reflecting optimal performance

Performance on all tests represented as standard scores with higher scores reflecting optimal performance.

Impressions and Recommendations

- Autoimmune encephalitis
  - Further treatment planning deferred to neurology
- Functional neurological symptoms
  - Consider psychotherapy for stress management and coping skills
  - Mindful return to school
Eight Months Later

- Enrolled in public school
- Non-competitive gymnastics club
- Noticeable improvements in voice and mannerisms
- Family complaints of residual mild memory deficits
- All other symptoms resolved

Lessons Learned

- Assessment of rare neuroimmunological disease is inexact and ever-evolving, particularly in pediatrics
- Functional neurological symptom exacerbation can be considered alongside medical etiology
- Multidisciplinary collaboration can promote the best outcomes for patients and families
Pediatric Grand Rounds

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