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Case Report

# Hemolytic Anemia and Short-term Memory Decline: A Case Study

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## Abstract

Hemolytic anemia and immune thrombocytopenia (ITP) have been associated with many symptoms including fatigue and cognitive dysfunction. Hemolytic anemia causes diminished hemoglobin production and thus potentially reduces oxygen transportation to organs and the brain. This case presentation discusses a 36 year old woman (Ms. T) who was very healthy until she woke one morning with bruising and petechiae all over her body. In the emergency department, she was diagnosed with ITP and treated with IVIG and brief chemotherapy. She then developed hemolytic anemia and various symptoms including fatigue, weakness, and cognitive decline. Specifically, she experienced a brief delirium and this was followed by persistent memory impairment. After receiving numerous blood transfusions, Ms. T developed hemochromatosis. As the anemia resolved, her cognitive impairments, particularly short-term memory, persisted with limited improvement for over a year. However after three months of cognitive rehabilitation, which was initiated more than one year post resolution of her anemia, Ms. T showed significant improvement in short-term memory and was generally functioning better in her community.

## Introduction

Many medical disorders indirectly affect brain functioning including cognitive skills. In the case discussed in this manuscript, the person developed immune thrombocytopenia (ITP) that was treated with IVIG. Subsequently, the person developed hemolytic anemia and cognitive impairments became most apparent at that time. The treatment of the anemia involved many transfusions leading to hemochromatosis. The hemochromatosis did not produce significant symptoms, other than skin discoloration, and this disorder was still present after successful cognitive rehabilitation.

### Immune Thrombocytopenia (ITP)

Immune thrombocytopenia (ITP) is defined as an isolated low platelet count (thrombocytopenia) with normal bone marrow [1]. It is an autoimmune disease with antibodies detectable against several platelet surface antigens. A diagnosis of ITP is considered if the platelet count is lower than 100,000/microliter of blood (150,000-400,000 normal range) and other causes have been excluded. First, it has to be determined that there are no blood abnormalities other than a low platelet count and no physical signs other than bleeding. Secondary causes (5–10 percent of suspected ITP cases) should then be excluded. Such secondary causes include leukemia, medications (e.g., quinine, heparin), lupus erythematosus, cirrhosis, HIV, hepatitis C, congenital causes, antiphospholipid syndrome, von Willebrand factor deficiency, and various other disorders [2].

ITP often has a characteristic purpuric rash and the person has an increased tendency to bleed. Two distinct clinical syndromes manifest as an acute condition in children and a chronic condition in adults. The acute form often follows an infection and has a spontaneous resolution within two months. Chronic immune thrombocytopenia persists longer than six months with a specific cause being unknown [1,2].

Low platelet levels have been implicated in memory disorders but this has not been investigated in patients with immune

or idiopathic thrombocytopenia (ITP). Some empirical research comparing people with ITP (n=398) and controls found that people with ITP exhibit more autonomic dysfunction and also more memory impairment. Despite these findings, the memory impairment did not correlate with platelet count and the mechanism of action seems unclear. This research suggests that autonomic dysfunction may be one of the causal or contributing factors [3].

Ahn and colleagues [4] studied 23 ITP patients and found several common symptoms including recurrent dizziness, TIA like symptoms, memory loss and other cognitive impairment. It was speculated that ITP may cause small vessel disease and in some individuals it may increase the risk of dementia.

## Hemochromatosis

Hemochromatosis is the excessive accumulation of iron in body organs. Absorption, transport, and storage of iron are both essential and potentially toxic if not well regulated by the body. There is evidence associating excessive iron and neurodegenerative diseases [5]. Some research suggests the possibility that hemochromatosis may interact with apolipoprotein E4 allele and may present a risk factor for early onset Alzheimer's Disease [6].

## Hemolytic Anemia

Hemolytic anemia causes a significant decline in functional hemoglobin and thus potentially reduces oxygen transportation to organs and the brain. Anemia can cause hypoxia and this has been shown to negatively affect physical functioning, cognitive performance and mood [7,8]. Several empirical studies suggest that anemia symptoms may be due to low level hypoxia.

## Case Study

When trying to conceptualize a case and plan the most effective treatment regime and recommendations it is often essential to piece together a complex medical history in a sequential manner with some attention to the timeline and temporal relationships. Following is a summary of Ms. T's medical and treatment history.

Ms. T was 33 years old, married, healthy, and working more than 40 hours per week at an animal shelter. She woke up one morning with petechiae and bruises all over her body. She physically felt fine, but went to the emergency department at a local hospital for the bruising and was admitted.

She was diagnosed with ITP and was started on prednisone and transfusions for 8 days, but her platelets remained below 20,000. She was then started on IVIG and her platelets increased to 50,000, at which time she was discharged from the Intensive Care Unit. Her platelets then went up to 99,000 and she was discharged home. A day after discharge, she developed a headache and was taken back to the emergency department where she was diagnosed with migraines, but not admitted. She went home, became jaundiced and experienced a notable decline in cognitive functioning.

She was then brought back to the emergency department and was found to have hemolytic anemia. Medical records report that Ms. T was admitted to inpatient care with "catastrophic haemolytic anemia with haemoglobin (HGB) as low as 1.6 (female norms =12-16 dm/gl), thought to be a side effect of IVIG and ITP." The hospital course was protracted due to acute renal failure requiring dialysis, liver failure, and multiple blood transfusions. Though ITP may place someone at risk for a stroke or TIA, Ms. T was not thought to have either. TIA and stroke often have abrupt, lateralized symptom presentations [9]. Her acute symptoms were not lateralized, rather were generalized, and included fatigue, jaundice, weight loss, easy bruising, irregular heartbeat, dizziness, and anxiety. Moreover her cognitive impairment was not apparent until she developed hemolytic anemia. Secondary to the multiple blood transfusions, Ms. T developed hemochromatosis. She was discharged after a seven week hospitalization.

After being discharged from inpatient care, Ms. T had a much lower activity level than before her medical issues. She reportedly was very weak, could barely walk household distances, and had lost a significant amount of weight, including much of her strength from her limited activity and significant time in a hospital bed. Besides her physical symptoms, Ms. T reportedly had a very limited attention span and a significant loss of short-term memory. These cognitive symptoms were thought to be secondary to her significant anemia and potentially related hypoxia. Mild or more severe cerebral hypoxia has been associated with memory impairments, attention issues, and possible executive dysfunction and motor impairment [10].

Initially, Ms. T's memory loss was sufficiently severe to be disabling and she struggled to function even with routine household activities. After 6 months at home she started to feel more energetic and experienced some spontaneous recovery of memory and decided to seek treatment for her cognitive dysfunction.

Ms. T presented for post-acute outpatient cognitive rehabilitation at more than one year post her cognitive decline. She was evaluated for a post-acute brain injury rehabilitation program and was admitted for 3 months of treatment. At time of admission, Ms. T was medically stable except for her hemochromatosis and was receiving month phlebotomies for that condition. At admission, she reported continued forgetfulness during daily and weekly activities. She felt it may involve some attention issues, but largely involved forgetting things. On admission, objective brief neuropsychological testing, using the Repeatable Battery for the Assessment of Neuropsychological Functioning (RBANS), showed a mild impairment in short-term memory (see Table 1). Reading was measured using the Wide Range Achievement Test-4 (WRAT-4) and used at time of admission as an objective estimate of premorbid intellectual

| Memory Measures Administered | Intake Assessment (percentile) | 4 weeks into treatment (percentile) | Discharge Assessment (percentile) |
|---|---|---|---|
| WRAT-4 Word Reading | 79 | -- | -- |
| RBANS-Immediate Memory | 5 | 16 | 63 |
| Delayed List recall | 2 | 50 | 50 |
| List Recognition | 2 | 9 | 16 |
| Story Recall | 5 | 63 | 63 |
| Wechsler Memory Scale-IV: Logical Memory-I | -- | -- | 91 |
| Wechsler Memory Scale-IV: Logical Memory-II | -- | -- | 91 |
| Verbal Paired Associates-I | -- | -- | 95 |
| Verbal Paired Associates-II: Delayed recall | -- | -- | 37 |
| Verbal Paired Associates-II: Recognition | | | 75 |

**Table 1:** Neuropsychological test results at admission to and discharge from a post-acute rehabilitation program for brain injury.

functioning, which was significantly above average. Her admission memory test scores ranged from the 2nd to the 5th percentile and were suggestive of moderate impairments. This sharply contrasts with her estimate of premorbid functioning and her discharge assessment which shows consistently above average short-term memory scores. Her short-term memory appeared to fully, or nearly fully, recover.

Her memory improvement was measured during the course of rehabilitation and at the time of discharge via an objective memory measure (RBANS) which demonstrated improved short-term memory. Findings of improved memory on the RBANS at discharge were corroborated by a second objective memory measure (Wechsler Memory Scale – IV) that placed her performance in the average to above average range. Her short-term memory improvements were evident both at 4 weeks post treatment onset and at the time of discharge (3 months after treatment onset). Table 1 provides scores are provided as percentiles (average range = 25th to 73rd percentile). As Ms. T neared her treatment discharge she was experiencing improved functioning at home and in her community and was considering future vocational and other activities that she had discontinued after her decline.

The brain injury rehabilitation program which Ms. T participated in involved the following interventions: 2 hours per week of each of Speech Therapy, Occupational Therapy, Physical Therapy, and Neuropsychology (cognitive rehabilitation) consultations. The cognitive rehabilitation for her memory involved developing and consistently using memory compensatory strategies. Her treatment also involved various memory exercises involving encoding skills, semantic and elaborative encoding, and attending to and organizing information more effectively. Ms. T also participated in a Wellness group and groups to promote improved coping and emotional adjustment.

Retraining of memory function is based on the supposition that impaired memory will respond to mental exercise [11]. Thus, memory was addressed in rehabilitation utilizing both external and internal memory strategies. The rationale behind the use of these strategies is to regain memory through the improvement of encoding and retrieval. Such improvement is thought to be the product of a combination of forced-use paradigm and diverse encoding strategies. The encoding strategies may include employment of cognitive strengths and engagement of different parts of the brain than those previously used to encode information. Additionally, imagery may be used to enhance the encoding of verbal information. Elaborative encoding strategies might facilitate retention and retrieval of information [12].

## Discussion

This case highlights many clinical issues. For example, it highlights the potential of iatrogenic effects of some efficacious medical treatments. Ms. T developed anemia after several rounds of IVIG and she developed hemochromatosis after several blood transfusion. Her cognitive symptoms were thought to be caused largely by the haemolytic anemia though it appears possible that her ITP may have been a contributing factor. One of the more important aspects of this case is that this person showed evidence of full cognitive recovery long after she developed cognitive impairments, particularly in the area of short-term memory. Consistent with common beliefs, it was suspected that Ms. T's cognitive impairments persisted beyond the time period of either natural spontaneous recovery or potential efficacy for cognitive rehabilitation. In retrospect, it seems plausible that she suffered some level of disrupted neurophysiology (likely due to anemia/hypoxia) that did not manifest in structural defects that could be found on CT (MRI was not completed). Ms. T showed significant improvement in cognitive functioning as measured by neuropsychological tests after three months of treatment (and many months post symptom onset) and this seems to suggest that some neuropsychological symptoms secondary to ITP/hemolytic anemia/hemochromatosis may be persistent, but not permanent. Alternatively or conjointly, effects of rehabilitation may result in markedly improved outcome in regard to memory functioning for this patient population. Because treatment involved increased physical and cognitive activity along with improved coping and support, it is not possible to solely contribute her improved memory entirely to the cognitive rehabilitation. It should be noted that functional memory improvements were also significantly improved as was overall functioning.

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