

# Neurologic Manifestations of Blood Dyscrasias



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## KEYWORDS

• Plasma cell • Dyscrasia • Myeloma • Neuropathy • Radiculopathy

## KEY POINTS

- Neurologic manifestations are common in both benign and malignant disorders, and they can affect both central and peripheral nervous system.
- The most common neurologic manifestations in blood cell dyscrasias are those involving the peripheral nervous system.
- Anemias, particularly B<sub>12</sub> deficiency and sickle cell disease, lymphomas, leukemias and myelomas are the diseases more frequently associated with neurological manifestations.

## INTRODUCTION

Neurologic manifestations are common in blood diseases, and they can be caused by the hematologic disorder or its treatment.

This article discusses hematologic diseases in adult patients, and categorizes them into benign and malignant conditions. The more common benign hematologic diseases associated with neurologic manifestations include anemias, particularly caused by B<sub>12</sub> deficiency and sickle cell disease, and a variety of disorders of hemostasis causing bleeding or thrombosis, including thrombotic microangiopathy (TMA). Malignant conditions like multiple myeloma (MM), leukemias, and lymphomas can have neurologic complications resulting from direct involvement, or caused by the different therapies to treat these cancers.

A classification of the most important hematologic conditions associated with neurologic complications or manifestations is presented in **Box 1**. This article gives a brief overview of these conditions, because they are developed in depth throughout this issue.

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### Box 1 Hematologic disorders

#### *Benign hematologic conditions:*

1. Anemias:
  - a. B<sub>12</sub> deficiency, folate deficiency
  - b. Sickle cell disease
  - c. Paroxysmal nocturnal hemoglobinuria
2. Disorders of hemostasis:
  - a. Hemorrhagic disorders: hemophilia A and B, disseminated intravascular coagulation (DIC), thrombocytopenias, and disorders of platelet function
  - b. Thrombotic disorders: antiphospholipid antibodies, inherited thrombophilia (eg, antithrombin III, protein C or S deficiency, factor V Leiden)
  - c. Other: thrombotic microangiopathies (eg, thrombotic thrombocytopenic purpura, hemolytic-uremic syndrome)  
DIC

#### *Malignant hematologic conditions:*

1. Leukemia
2. Lymphoma
3. Myeloma
4. Treatment of hematologic conditions

## BENIGN HEMATOLOGIC CONDITIONS

### *Anemias*

Iron deficiency anemias are frequently associated with nonspecific symptoms like fatigue, weakness, irritability, dizziness, tinnitus, and headache. Pseudotumor cerebri and cerebral venous sinus thrombosis have also been associated with iron deficiency. However, thrombotic episodes are likely to be associated with the thrombocytosis that occurs in iron-deficient patients; this can sometimes be severe and cause cerebrovascular infarction or transient ischemic attacks (TIAs). In patients with preexisting severe vascular disease, anemia can contribute to cerebrovascular or cardiac events that usually reverse with an increase in hemoglobin.<sup>1,2</sup>

Vitamin B<sub>12</sub> deficiency can cause neurologic symptoms even in the absence of appreciable alterations in peripheral blood and with normoblastic hematopoiesis. Furthermore, the size of the red cells can be within normal limits, because some of these patients have coexisting iron deficiency. Thus, methylmalonic acid and total homocysteine levels may be useful adjuncts in the diagnosis. Sensory peripheral neuropathy and myelopathy can occur because of loss of large, myelinated fibers, and axonal degeneration. Neuropathy usually has upper-limb onset and associated Lhermitte phenomenon. Myelopathy is accompanied by early and severe impairment of proprioception and vibration sense. Other less common forms of neurologic involvement, like sensory ataxic spastic paraparesis and optic neuropathy, have also been described. Encephalopathy with unspecified mental status changes or affective disorders have been found in about 20% of patients with B<sub>12</sub> deficiency.<sup>3,4</sup> Folate deficiency is a more common cause of neurologic disease in children, in whom it typically presents with seizures, delayed motor and cognitive development, cerebellar ataxia, spasticity, and visual and hearing impairment. Subacute combined degeneration of the cord accompanying diet-induced folic acid deficiency may occur and can improve with replacement.<sup>5,6</sup>

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