

## Review Article

# Clinical features, diagnosis, and types of optic neuritis

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## ABSTRACT

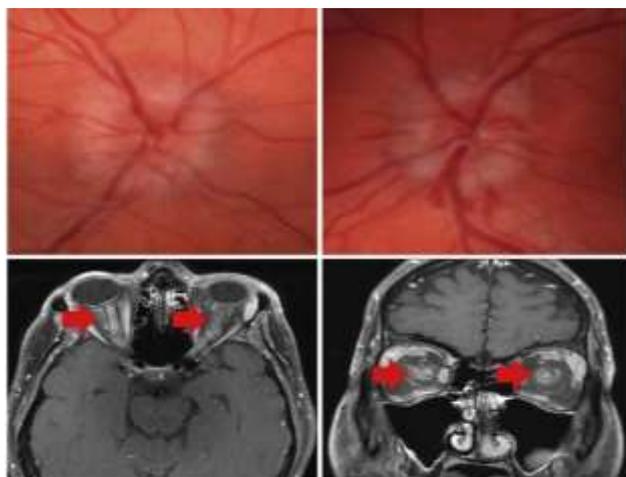
Establishing a proper diagnosis and identifying the underlying etiology of optic neuritis can be challenging in clinical settings. This is due to the various subtypes and etiologies that were reported for the condition. However, conducting a thorough examination and the laboratory and imaging modalities can significantly enhance the diagnosis. Therefore, it is essential to be adequately aware of the different subtypes of optic neuritis and distinguish between the different clinical features and diagnostic findings of each subtype to conduct a proper diagnosis and enhance management of the affected cases. Optic neuritis is a severe condition that can lead to permanent vision loss. In the present literature review, we have discussed the potential clinical features and diagnostic findings of the different types of optic neuritis. More severe cases of optic neuritis are usually associated with NMOSD and IgG-MOG cases with a worsened prognosis. Painless and chronic vision loss might occur secondary to infections and granulomatous diseases. On the other hand, optic neuritis secondary to multiple sclerosis is usually self-limited. Many of the cases of optic neuritis are characterized by being responsive to steroid therapy. However, acute vision loss was also reported in some cases. Therefore, clinicians must be knowledgeable enough to conduct the most appropriate diagnostic and management modalities to enhance the prognosis of the affected patients. Further research is needed for optimizing the treatment plan and drawing better interventions.

**Keywords:** Optic neuritis, Systemic diseases, Diagnosis, Clinical presentation, Optic nerve disease



### MOG-positive and NMOSD-induced optic neuritis

Estimates show that this condition is usually bilateral (ranging between 37 to 44% of the cases), has no ethnic differences, and is more common among females (with an estimated rate of 57%).<sup>18,19</sup> Studies also show that the age of onset of the condition is variable and the clinical features might vary based on the age of the affected patients. For instance, it has been shown that unilateral optic neuritis is more common among patients aged 20-45 years old. On the other hand, it has been reported that bilateral optic neuritis is more common among older adults. In addition, estimates show that in 25% of the affected cases, a concurrent presence of transverse myelitis-like NMOSD and optic neuritis is usually detected. In children, recurrent optic neuritis and acute disseminated encephalomyelitis (ADEM) are the main presentations of IgG-MOG condition.<sup>18,19</sup> Previous studies have reported that the associated vision loss in these cases is usually characterized by optic disc edema, being painful and severe (in 86% of the cases).<sup>18,20</sup> Perineural enhancements and extensive longitudinal optic nerve lesions are the most common MRI findings of IgG-MOG-induced optic neuritis, affecting 50% and 80% of the cases, respectively (Figure 2). It has been furtherly demonstrated that the condition is usually steroid dependant and also responds to steroid treatment. Besides, estimates indicate that the incidence of developing severe vision loss is rare when the underlying pathology has been observed once. Accordingly, the high rate of severe vision loss is attributed to recurrent episodes of optic neuritis.<sup>19,20</sup> Optic neuritis has been reported among patients with seropositive and negative QP4-IgG NMOSD patients.<sup>21</sup> MRI can show diagnostic findings. However, it has been demonstrated that optic edema is usually rare. Moreover, vision loss might be associated with 20% of the cases and is usually bilateral and severe.<sup>22-24</sup> CSF findings are also abundant in the affected patients. It has been demonstrated that QP4-IgG seropositive patients are at increased risk of recurrence.<sup>21</sup>



**Figure 2: MRI findings and fundus imaging of a case of optic neuritis with positive myelin oligodendrocyte glycoprotein antibody.**<sup>19</sup>

### Recurrent idiopathic optic neuritis

The first report of autoimmune optic neuritis was first introduced to the literature by Dutton et al.<sup>25</sup> The clinical characteristics of the condition include infrequent painful sensation and mild-to-moderate loss of visual acuity. Mild edema might also manifest on fundus examination. Imaging and laboratory investigations have been reported to be of limited value. However, evidence shows that cardiolipin antibodies and antinuclear antibodies (ANA) are usually found in the affected patients. In addition, it has been reported that histopathologic vasculitis might be detected by skin biopsy (25%). In other cases, complement deposition, immune complex, and immunoglobulins are usually found.<sup>26</sup> Bilateral or unilateral, spontaneous unresponsive attacks and isolated optic neuritis has been reported with relapsing isolated optic neuritis<sup>27</sup>. Females are predominantly affected, and evidence shows a low rate of systemic involvement (14%). Moderate vision loss was also reported in these cases (20/80).<sup>28-30</sup> Reports also show that CSF oligoclonal bands and pleocytosis are not commonly found. Moreover, ANA can be detected in 15% of the cases only.

On the other hand, it has been demonstrated that the presence of progressive vision loss together with recurrent isolated attacks of bilateral unilateral optic neuritis refers to chronic relapsing inflammatory optic neuropathy.<sup>31</sup> The condition was primarily reported as steroid-dependant. However, more recent evidence shows that prevention requires the administration of immunosuppressive modalities. It has been furtherly demonstrated that patients usually have severe vision loss. Other characteristics are similar to the ones reported with relapsing isolated optic neuritis.<sup>27,31,32</sup>

### Optic neuritis owing to systemic conditions

Evidence shows that optic neuritis usually develops as a paraneoplastic condition, which is also correlated with CRMP-5/CV-2.<sup>33</sup> The condition is usually found in cases of small cell carcinoma. However, it has been reported that other tumors might also induce optic neuritis, including thymoma, lung adenocarcinoma, renal cell carcinoma, and prostate cancer.<sup>33,34</sup> The reported vision loss in these cases usually develops within weeks or months, progressive, and subacute. However, the condition is not painful. Fundus examination might indicate the presence of optic disc edema, vitritis, and associated hemorrhagic features. In addition, the disease is usually associated with other central and peripheral manifestations that can help with the condition's diagnosis.<sup>35</sup> Systemic lupus erythematosus (SLE) can also predispose to the development of isolated optic neuritis. However, estimates indicate that the condition is not common in these events.<sup>36,37</sup> This has been displayed in a previous investigation, which showed that only 4.3% of cases with SLE have CNS involvement. Among these cases, it has been reported that optic neuritis is present in

8.7% of them. The condition is usually severe with incomplete recovery.

Moreover, a worse prognosis can be elicited by the presence of associated antiphospholipid or vasculitis disorders. This might be detected by potentially observing ischemic anterior optic neuropathy and optic disc edema.<sup>38,39</sup> Optic neuritis was also reported with patients with Sjögren syndrome. However, evidence indicates that CNS involvement in these cases is usually rare (5%), and optic neuritis is usually reported in 4% of these cases.<sup>40</sup> Recurrence has been reported in around one-third of the affected patients, and evidence indicates that the prognosis of the condition is variable. At the same time, most cases can be treated with corticosteroids. In these patients, evaluating the presence of AQP4 autoantibodies should be conducted in cases when NMOSD is associated.<sup>39</sup>

#### *Optic neuritis wing to infections and granulomatous disorders*

Various infections can predispose to the development of optic neuritis. The most common conditions include neuroretinitis, which has been reported secondary to many bacterial and viral infections.<sup>41</sup> Vision loss is usually painless and central. Therefore, OCT might be diagnostic, and most cases resolve spontaneously.<sup>41,42</sup> Lyme disease, syphilis, and tuberculosis were also reported to predispose to the development of optic neuritis.<sup>43</sup> CSF analysis might be of great value in cases with syphilis. It usually shows intrathecal IgG synthesis, elevated protein levels, and lymphocytic pleocytosis. Optic neuritis was also reported secondary to different viral infections. These include rubella, measles, mumps, dengue fever, West Nile virus, HIV, Epstein-Barr virus, cytomegalovirus, varicella-zoster virus, and herpes simplex virus.<sup>44</sup> Many of these infections affect immunocompromised patients, and evidence shows that many of them might respond to corticosteroid therapy. Moreover, it has been reported that vision loss is usually bilateral in cases with cytomegalovirus and Epstein-Barr viral infections. Accordingly, the clinical characteristics of the affected patients should be evaluated according to the underlying etiology.<sup>43</sup>

Optic neuritis secondary to granulomatous diseases was also evidenced in the literature. For instance, in cases with granulomatosis with polyangiitis, it has been reported that optic neuritis might be present. The disease is usually bilateral, and vision loss is severe. The reported characteristics of the condition include diplopia, occlusion of the central retinal vein, chorioretinal ischemia, vasculitis. Other features include vitreitis, uveitis, orbital cellulitis, dacryoadenitis, and ulcerative conjunctivitis.<sup>45,46</sup> Optic neuritis might also be associated with sarcoidosis. In these events, evidence shows that around half of cases are unilateral and bilateral cases are usually asynchronous. Retinal vasculitis (also known as candle-wax droppings), macular exudates, infarcts to the

nerve fiber layer, and vitreitis are frequently observed changes. CSF and MRI can also add to the diagnostic value of the condition.<sup>47,48</sup>

## CONCLUSION

Optic neuritis is a severe condition that can lead to permanent vision loss. In the present literature review, we have discussed the potential clinical features and diagnostic findings of the different types of optic neuritis. More severe cases of optic neuritis are usually associated with NMOSD and IgG-MOG cases with a worsened prognosis. Painless and chronic vision loss might occur secondary to infections and granulomatous diseases. On the other hand, optic neuritis secondary to multiple sclerosis is usually self-limited. Many of the cases of optic neuritis are characterized by being responsive to steroid therapy. However, acute vision loss was also reported in some cases. Therefore, clinicians must be knowledgeable enough to conduct the most appropriate diagnostic and management modalities to enhance the prognosis of the affected patients. Further research is needed for optimizing the treatment plan and drawing better interventions.

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