Is there a link between hematologic malignancy and ischemic optic neuropathy?

Ischemic optic neuropathy is the most common acute optic neuropathy in patients over the age of 50. The ischemic injury may be localized to the anterior part of the optic nerve – anterior ischemic optic neuropathy (AION), or to its retrobulbar portion – posterior ischemic optic neuropathy. The most common (90-95%) form - non-arteritic AION (NAION) - results from ischemia of the optic nerve head in patients with cardiovascular risk factors, such as obesity, arterial hypertension and diabetes mellitus.

Previous studies have estimated the prevalence of systemic diseases that might predispose to NAION, and patients with hematologic malignancies may share demographic and clinical features with NAION patients. Our objective was to systematically review previously published cases of hematological malignancies related in time with NAION, discussing its potential implications.

Number of cases	19 (8 female)
Mean Age	55 years (range 12-87)
Neoplasm subtype	7 (37%) NHL
	5 (26%) MPN
	4 (21%) MDS
	3 (16%) Leuk
Neoplasm outcome	9 (47%) died within a year
	7 (37%) remission
	3 (16%) non specified
Ophthalmologic symptoms related to neoplasm diagnosis	10 (53%) following neoplasm diagnosis
	8 (42%) before neoplasm diagnosis
	1 (5%) non specified
Visual acuity in the affected eye(s) after follow-up	6 (32%) improved
	5 (26%) equal
	4 (21%) worsened
	4 (21%) lost to follow-up

Tab. 1.

Although based on an underreported sample of the number of patients with either condition, these results of our study describe the demographic and clinical characteristics of a cluster of patients who share the diagnosis of both a NAION and a hematologic neoplasm (Tab. 1). For all the 19

patients included and described in this systematic review there was a clear relation in time between these entities.

Which comes first: optic neuropathy or the hematologic neoplasm?
Intriguingly, eight (42%) patients had NAION diagnosed before the diagnoses of their hematologic neoplasm [range: 10 days - 4 months). However, this may be inaccurate in the sense that the NAION could be a manifestation of a still non-diagnosed hematologic neoplasm. This finding raises the hypothesis of the potential for earlier diagnosis of hematological disease following an optic nerve ischemic event.

Is NAION and hematologic neoplasms different to isolated NAION?
Remarkably, in this review, thirteen (68%) patients with NAION did not present the typical cardiovascular risk factors for its occurrence. Also, only one patient was described to have a crowded optic disc (an anatomical risk factor). Last but not least, simultaneous or sequential bilateral NAION was identified in 9 (47%) and 4 (21%) patients, respectively. This trend for common bilateral disease is not common in published literature. In this regard, one must have in mind that a bilateral NAION without typical risk factors may be a presenting manifestation a hematologic neoplasm.

Limitations of methodology
However, our conclusions are inevitably limited due to the limited number of patients identified in this study design. Moreover, the fact that this study was based on case reports and case series is a source of possible bias, namely verification bias. A case-control study would likely be the optimal study design to investigate the association between these two diseases. Additionally, it is also important to investigate if the hematologic disease could be related with the ophthalmologic prognosis. This could be of invaluable significance for better management, in terms of follow-up and therapeutics. And lastly, as a methodological definition, systematic reviews cannot establish a statistical association, in this case between NAION and hematological neoplasms.

Implications for clinical practice and clinical research
The diagnosis of NAION related in time in hematologic neoplasms may be considered a rare presentation of a frequent group of diseases - hematologic neoplasms.

This review identifies the clinical characteristics of patients with NAION and hematological neoplasms related in time. Further observational studies may enlighten the importance of looking for evidence of an occult neoplastic disorder in patients presenting with NAION. Contemporary medical care in developed countries invests a lot in diagnostic testing, to detect disease as early as possible and, hence, increasing chances of treating it effectively.

Still, clinical examination and medical history are more accessible, many times simpler and assuredly cheaper. Using the best scientific and clinical knowledge, namely in disease screening and management, would be important in optimizing the care provided for these patients, from

diagnosis to treatment.

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