J Neurol (2002) 249 : 1713 – 1716
DOI 10.1007/s00415-002-0919-6

ORIGINAL COMMUNICATION

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Ocular manifestation of primary nervous system lymphoma: what can be expected from imaging?

Received: 17 April 2002
Accepted: 9 July 2002

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Abstract Primary ocular lymphoma, which affects the posterior parts of the eye, is an ocular manifestation of primary central nervous system lymphoma (PCNSL). It used to be the ocular disease with the shortest time of survival, even worse than ocular melanoma. Death ensues by CNS dissemination. Unfortunately, ocular lymphoma may be the initial manifestation of PCNSL and diagnosis is frequently difficult, even if vitreal biopsy is performed. Therefore, it should be determined whether cross sectional imaging may be helpful in detection and differential diagnosis of ocular lymphoma.

MRI of seven patients (female = 6, male = 1, median age 62 years) with biopsy proven ocular lymphoma were retrieved from the files of our hospital and of a multicenter PCNSL study. In four patients, ocular lymphoma was the first manifestation of PCNSL, in three a cerebral lesion had occurred in the first place. Progression to cerebral lymphoma was seen in three of the four patients with initial eye manifestation.

Imaging was performed using a dedicated thin section protocol in four patients. An intraocular abnormality was found in four cases, always in T1-weighted images after contrast injection. Differential diagnosis from uveitis or ocular melanoma was not possible by imaging alone. The examination was falsely negative in the remaining three patients.

Hence, imaging has a low sensitivity for ocular lymphoma and does not facilitate differential diagnosis against uveitis or ocular melanoma.

Key words primary central nervous system lymphoma · MRI · uveitis · ocular manifestations

Introduction

Primary central nervous system lymphoma (PCNSL) is a rare neoplastic disease of the brain, spinal cord or the eye. PCNSL are derived from B-cells in the vast majority of cases. The incidence of this disorder was reported to be 0.43:100 000 [7, 10]. However, cerebral lymphoma seems to have become more frequent in recent years [2]. It has been estimated that between 1 and 6 % of all CNS neoplasms are PCNSL [8]. In contrast to former reports, new chemo- and radiotherapy strategies have significantly increased survival and quality of life in this group of patients [3–5].

In cerebral and spinal cord lymphoma, diagnosis depends on imaging, biopsy and CSF cytology. Because surgical resection does not improve the prognosis of PCNSL, it should be avoided. MRI signs of PCNSL have recently been reported by several groups [1]; however, in the majority of cases biopsy still remains necessary. His-

tological verification should be attempted before medication is begun because steroid treatment may severely hamper morphological diagnosis.

PCNSL is a systemic disorder of the central nervous system. The most frequent localisation is the brain itself. Primary lymphoma of the spinal cord is rare [6]. Ocular lymphoma has a lower incidence than intracerebral manifestation but is more frequent than spinal cord PCNSL. The diagnosis of ocular lymphoma relies on ophthalmological inspection and vitreal biopsy. It mostly presents as steroid-resistant uveitis and used to be the most fatal ophthalmological disease. However, biopsy may be falsely negative in up to 30 %. Therefore imaging is frequently performed to rule out other forms of pathology and to search for further manifestations of PCNSL in the brain and spinal cord. This finding would obviate the need for a purely diagnostic ophthalmological operation.

Up to now, no systematic evaluation of the imaging signs of ocular lymphoma has been performed. We report imaging signs of 7 patients with biopsy proven PCNSL.

Material and methods

Imaging studies of 7 patients (female = 6, male = 1, mean age = 62 years) with intraocular lymphoma were analysed in retrospect.

Imaging was performed before a cerebral manifestation was encountered in 4 cases and after the diagnosis of cerebral lesions was made in 3 patients. Diagnosis was confirmed by vitreal biopsy in 3 cases, by brain biopsy in 4 patients. With one exception, all patients with primary lymphoma of the eye have developed a brain manifestation. The follow-up time for the patient with isolated eye involvement was 6 months only. Dedicated thin section orbital examinations were done in 4 patients. Thin section MRI was performed on various MR systems with field strengths between 0.5 and 1.5T. All examinations encompassed thin section (3mm) T1-weighted images after administration of intravenous contrast agent (Gd-DTPA). T2-weighted thin section images were performed in 3 cases (Table 1). In addition to the orbital scans, whole brain examinations were performed to exclude cerebral manifestation of PCNSL. A thin section CT of the eye was done once, without contrast administration. In 3 patients with an established diagnosis of PCNSL, whole brain examinations were performed for treatment assessment. Ocular lymphoma was diagnosed clinically in these cases.

Results

Imaging abnormalities were seen in four patients with ocular lymphoma. All patients had an abnormal thickening of the uvea with pathological contrast uptake. The extent of this mass lesion ranged from a very circumscribed lesion at the macula, which was hardly visible in dedicated CT and MRI (Fig. 2), to an extensive involvement of the uvea in another patient (Fig. 1). A T2-signal abnormality could be detected in the patient with an extensive lymphoma lesion. The lesion was hypointense in the T2-weighted sequence. Probably because of eye movement, partial volume effects and a long T2 time, intraocular lymphoma remained mostly invisible in T2-weighted images.

CT did show a hyperdense lesion once, but without

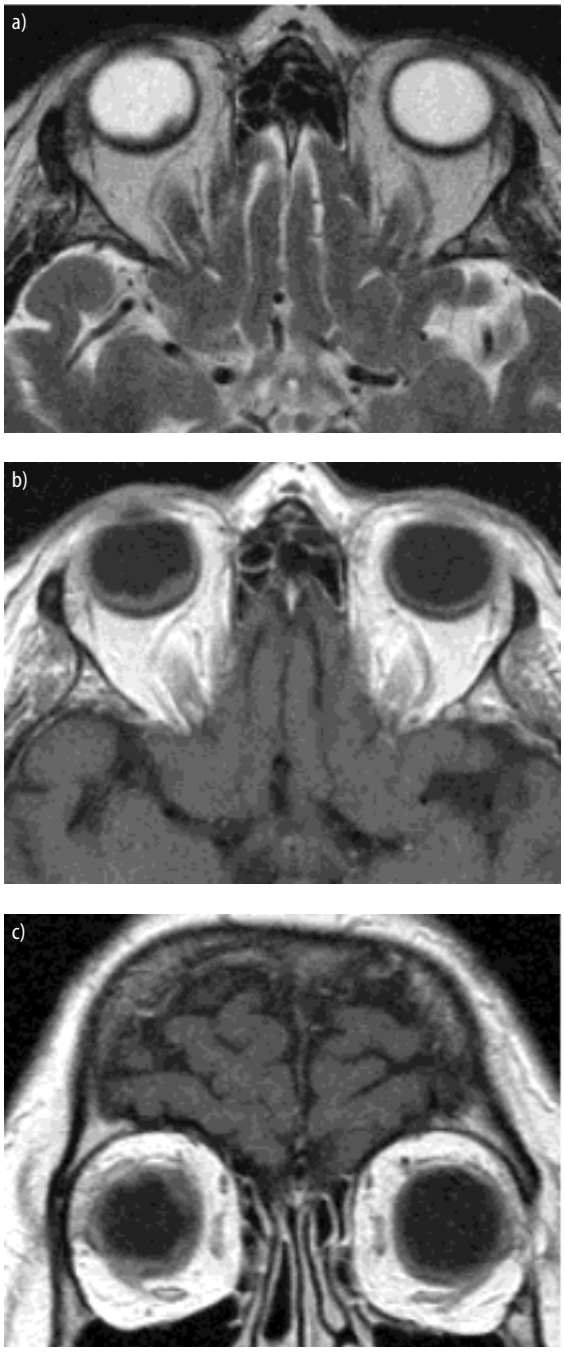

Fig. 1 (**a**) T2-weighted thin section image of the orbit (slice thickness = 3mm). There is a hypointense lesion in the right eye adjacent to the posterior wall of the bulbus. (**b**) T1-weighted image (slice thickness = 3mm) of the orbit after injection of Gd-DTPA. The mass in the dorsal part of the eye shows enhancement. (**c**) T1-weighted sequence (slice thickness = 3mm) after contrast administration. The circular intraocular mass lesion is clearly visible.

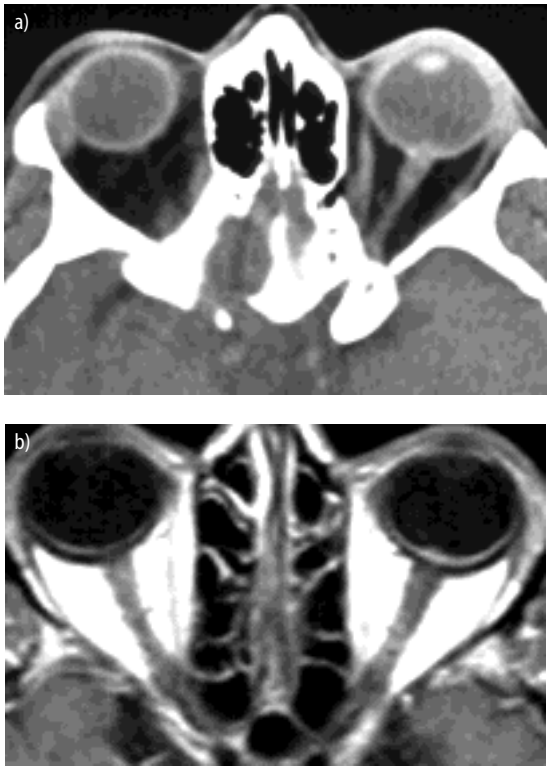

Fig. 2 (**a**) CT-scan through the left bulbus (slice thickness = 3mm). There is a slight hyperdense lesion in the left eye at the macula. Otherwise, the CT is normal. (**b**) This T1-weighted (slice thickness = 3mm) image of the same patient after contrast injection shows a very faint enhancement in the optic nerve entry zone.

characteristic features. Imaging studies did not show any ocular abnormality in three patients, although a dedicated orbital examination for clinically suspected ocular lymphoma was performed (Table 1). None of the patients presented here had an orbital lymphoma. Of the patients with initial presentation of ocular lymphoma, none had intracerebral lesions at the time of initial presentation.

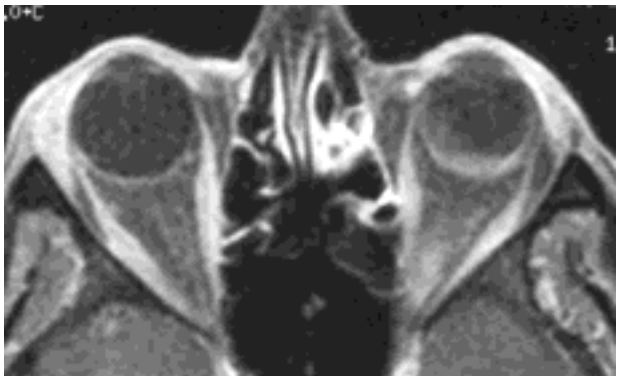

Fig. 3 This T1-weighted image with application of fat suppression (slice thickness = 3mm) after contrast administration shows a crescent shaped enhancing mass lesion in the dorsal part of the left eye. The T2-weighted image did not show an abnormality.

Discussion

Ocular lymphoma is a manifestation of PCNSL. The presenting symptom is a painless loss of vision in one eye. Bilateral involvement is encountered in 60–90 % in the course of the disease. Depending on the time of follow-up, 50–80 % of patients have been reported to develop cerebral PCNSL by ophthalmological authors. In the neurological literature the incidence of brain involvement is given as 23 of 24 patients in the largest series of patients [9]. The time interval between ocular manifestation and cerebral infiltration was reported to range from one month to 10 years with a mean of 20–30 months. Ocular disease precedes brain lesions in 50 to almost 100 % of cases.

Therefore, ocular lymphoma is a disseminated neoplastic disorder of the central nervous system and should be diagnosed and treated accordingly.

Unfortunately, diagnosis of ocular lymphoma may be even more difficult than in cerebral disease. Definite diagnosis usually requires vitreal biopsy. However, even this invasive procedure may be falsely negative in up to

Table 1

No	Initials	Age (years)	Sex	Initial manifestation	time to second manifestation	Imaging modality and sequences	Result of orbital imaging
1	L.A.	66	f	eye	second eye 6 months brain 12 months	Thin section T2& T1(Gd) CT	Lesion visible in T1 (Gd) and CT
2	E. B.	62	f	brain	4 months	Whole brain T1 (Gd)	Lesion visible in T1 (Gd)
3	E. J.	71	f	brain	2 months	Whole brain T1 (Gd)	Lesion visible in T1 (Gd)
4	B. K.	57	f	eye	–	Thin section T2& T1(Gd)	Lesion visible in T1 (Gd) and T2
5	H. K.	73	f	eye	4 months	Thin section T2& T1(Gd)	no lesion visible
6	C. H.	52	f	eye	3 months	Thin section T2& T1(Gd)	no lesion visible
7	F. K.	47	m	brain	4 months	Whole brain T1 (Gd)	no lesion visible

30 % of cases. Therefore, imaging is performed to gain further evidence for PCNSL before therapy is initiated. Radiation of the involved eye is a standard procedure. Furthermore, radiation of the contralateral eye is also performed owing to the high incidence of bilateral disease and chemotherapy is initiated to prevent cerebral involvement.

The purpose of this retrospective study was to find features indicative of PCNSL to support the tentative diagnosis with its far reaching implications.

Imaging was performed in four patients before a cerebral manifestation of PCNSL occurred. This is in line with literature reports. The patients usually presented with a steroid resistant uveitis. Imaging using a thin section orbital protocol detected an abnormality in two of these patients. The lesion presented as a nodular abnormality at the macula or as an extensive thickening of the uvea. In both of these cases, differential diagnosis was not facilitated by MRI. Because of the hypointensity in the T2-weighted sequence, the ocular lymphoma could not be distinguished from a melanoma in one of the patients. Two examinations were falsely negative.

In the remaining three cases, imaging was performed after the demonstration of a cerebral lymphoma. In these cases, the purpose of the study was to rule out any other form of ocular or orbital pathology. The imaging signs in the two patients with ocular abnormality did not differ from primary ocular lymphoma. One examination was falsely negative.

In conclusion, cross sectional imaging has a low sensitivity for ocular lymphoma, even if suspected clinically and if appropriate thin section orbital protocols are applied. If an intraocular abnormality is detected, it may resemble uveitis or melanoma. Therefore, the role of MRI in suspected ocular lymphoma is the exclusion of other forms of orbital pathology and the demonstration of concomitant, clinically asymptomatic cerebral PCNSL rather than the demonstration of the ocular pathology itself.

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