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Inflammatory optic neuropathy in Behçet's disease

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SUMMARY

Inflammatory optic neuropathy (ON) is a rare event in Behçet's disease (BD). We report herein a series of ten BD Tunisian patients with ON and describe its clinical features among them.

A retrospective review of BD patients (International Study Group for BD criteria) was performed. The patients were divided into two groups: those presenting an inflammatory ON, and those none. The diagnosis of inflammatory ON was based on the clinical examination, visual field and visual evoked potentials. We analyzed the characteristics of the two groups.

Ten patients (2.3%) presented an inflammatory ON among our 440 patients. Inflammatory ON was inaugural in 8 cases. Clinical manifestations were as follows: blurred vision (7 cases) and periorbital pain (3 cases). In two cases, the patients did not complain from ophthalmological symptoms. The fundus revealed a papilledema (2 cases), papillary pallor (4 cases), and was normal in 5 cases. Visual field realized in only three patients showed a scotoma in all cases. Visual evoked potentials revealed increased latency in all cases. All patients received corticosteroids associated to an immunosuppressive agent. The comparative study between the two groups revealed that inflammatory ON was significantly more associated to neurological involvement ($p<0.0001$) and that the disease was more severe in the ON group ($p<0.0001$).

Inflammatory ON in BD is rare and may occur at an early stage of the clinical course of the disease. Its prevalence is certainly underestimated. A systematic visual evoked potential may be interesting as a screening tool.

Key words: *Optic neuropathy; Behçet's disease; inflammation.*

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INTRODUCTION

Behçet's disease (BD) is a systemic condition of unknown cause affecting young adults in the Mediterranean area, mid-East and Japan (1). Its clinical features are known to differ among ethnics. Main ocular manifestations include uveitis, retinal vasculitis and papilledema (1-3). Optic neuropathy (ON) is rare in BD and seems to be misdiagnosed because of its association with ocular involvement (2, 4, 5). ON in BD belongs to the neuro-ophatalmic syndrome and is probably related to a vasculitic-mediated involvement of the optic nerve. This condition has to be systematically considered in BD patients with normal fundus and leads to start the treatment immediately because of the poor prognosis in those suffering from late diagnosis. Herein, we report retrospectively a series of ten Behçet's patients with inflammatory optic neuropathy, and we describe its clinical features and correlations with those without the disease.

MATERIALS AND METHODS

A retrospective review was performed concerning a well-documented population of Tunisian patients with Behçet's disease diagnosed from 1990 to 2010. All patients fulfilled three or more criteria as defined by the International Study Group for Behçet's disease (6). It requires the presence of oral ulceration plus any two of genital ulceration, typical defined eye lesions, typical defined skin lesions, or a positive pathergy test. The patients were divided into two groups: those with an inflammatory optic neuropathy and those without it. The inclusion criteria for an optic neuropathy were

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decreased and/or blurred vision, scotoma in the visual field, a relative afferent pupillary defect, optic disc edema or optic atrophy on fundus, and increased latency in visual evoked potentials. The exclusion criteria included secondary optic neuropathy due to cerebral venous thrombosis, ischemic anterior neuropathy, or glaucoma. We compared epidemiological, clinical, and evolutionary features in the two groups, using the statistics control test SPSS 18 (IBM Corp., Armonk, NY, USA).

RESULTS

Four hundred and forty patients were studied; their mean age at the beginning of the disease was 30 years at diagnosis. The mean delay to diagnose was five years. Three hundred and two (68%) were male and 138 (32%) female. Four hundred and thirty patients were excluded and 10 presenting an inflammatory optic neuropathy were included. The sex ratio (M/F) was 2.33. The mean age at the moment of the diagnosis of BD was 37.6 years. Inflammatory optic neuropathy was inaugural in 8 cases and happened in the course of the disease in two cases, within a period of 6 and 17 years. Inflammatory optic neuropathy was unilateral in 6 cases and bilateral in 4 cases. Clinical manifestations were as follows: blurred vision was reported in 7 cases and periorbital pain in 3 cases. Visual loss was rapidly progressive in 7 patients and brutal in one case. In two cases, the patients did not complain from ophthalmological symptoms and optic neuropathy was systematically discovered. The fundus was realized in all patients and revealed a papilledema in two cases, papillary pallor in 4 cases, and was normal in 5 cases. Retinal angiography showed in two cases an active vasculitis in which optic neuropa-

Table I - Clinical features of our Behçet's disease patients with inflammatory optic neuropathy.

Patient number	Sex	Age	ON: Clinical presentations	ON: Diagnostic delay	Associated ocular manifestations	Associated neurological manifestations	Fundus	Retinal angiography	Visual field	Visual evoked potentials	Prognosis
1	M	52	Progressive blurred vision	Inaugural	No	Cranial nerve palsy Pyramidal syndrome	Papillary pallor	Normal	Scotoma-quadranta-nopsia	Increasing latency	Stabilization
2	F	33	Progressive blurred vision	Inaugural	No	Pseudobulbar syndrome Pyramidal syndrome	Papillary pallor	Normal	Not done	Increasing latency	Stabilization
3	M	33	Brutal visual loss Ocular pain	Inaugural	Retinal vasculitis	Intracranial hypertension	Papilledema and pallor	Vasculitis	Not done	Increasing latency	Vision loss
4	M	53	Progressive blurred vision	17 years	Posterior uveitis	Pyramidal syndrome	Papillary pallor	Normal	Not done	Increasing latency	Stabilization
5	M	34	Progressive blurred vision	Inaugural	Panuveitis	No	Papilledema	Vasculitis	Not done	Increasing latency	Improvement of VA
6	F	26	Ocular pain Progressive blurred vision	Inaugural	No	Superficial sensory disturbance Sphincter dysfunction Pyramidal syndrome	Normal	Normal	Scotoma	Increasing latency	Improvement of VA
7	M	23	Asymptomatic	6 years	Anterior uveitis	Headache Meningeal syndrome	Normal	Normal	Not done	Increasing latency	Improvement of VA
8	F	31	Asymptomatic	Inaugural	Anterior uveitis	Pyramidal syndrome Cranial nerve palsy	Normal	Normal	Not done	Increasing latency	Improvement of VA
9	M	57	Progressive blurred vision	Inaugural	No	Pyramidal syndrome	Normal	Normal	Not done	Increasing latency	Stabilization
10	M	34	Progressive blurred vision Ocular pain	Inaugural	No	Pyramidal syndrome	Normal	Normal	Scotoma	Increasing latency	Lost of sight

ON, optic neuropathy; VA, vasculitis.

thy was concomitant to an ocular involvement. Visual field realized in only three patients showed a scotoma in all cases. Visual evoked potentials revealed increased latency in all cases. Cranial MR imaging was pathologic in 5/9 cases. All neuroradiologic findings were related to neuroBehçet and no specific lesions of the optic nerve were reported. Inflammatory optic neuropathy was associated to neurological involvement in 5 cases and to ocular involvement in one case. Both neurological and ocular involvement associated to optic neuropathy were reported in 6 patients. All patients received intravenous methylprednisolone (1g/day for 3 days) relayed by oral route prednisone (1 mg/kg/day) associated to 6 monthly pulses of cyclophosphamide (0.7 g/m^2 body surface), relayed by 1 mg/kg/day of azathioprine for a total duration of two years. Patient number 10 received steroids pulses and one cyclophosphamide infusion, then was lost of sight. The evolution revealed an improvement of visual acuity in four cases, a stabilization of the vision in 3 cases, and definitive vision loss in one case. One patient was lost of sight after discharge. Table I sums up the clinical presentation of our ten patients.

Table II sums up the epidemiological, clinical and evolutionary characteristics of the two groups of our Behçet's patients.

Optic neuropathy in our Behçet's disease patients was significantly more associated to neurological involvement (p<0.0001). The severity scale was significantly higher in the optic neuropathy group than in those without ON (p<0.0001).

DISCUSSION

The prevalence of inflammatory ON is not easily estimated among series. Optic nerve involvement in Behçet's disease varies among series and ethnicity. Table III sums up the prevalence of ON in the different series. It varies from 1% to 9% (7-11) including secondary ON such as cerebral thrombophlebitis, ischemic anterior neuropathy, and ocular hypertension. In our series, the prevalence of inflammatory optic neuropathy was 2.3%. We demonstrate that it occurs mostly in association with neurological involvement (90%, p<0.0001) and in severe courses of the disease (90%, p<0.0001). These data were previously reported in different series (Table III). That is to say that inflammatory ON is a rare manifestation but underestimated condition, probably due to associated uveitis. The importance of diagnosing ON is challenging because of the possibility of reversible damage in early diagnosed patients. Otherwise, the prognosis is poor with permanent blindness. In our case series, we could diagnose ON by realizing systematically visual evoked potentials in two patients with neurological involvement. This may be an interesting tool for the misdiagnosed inflammatory ON which may be totally asymptomatic as in our patients 7 and 8 (Table I). Only a handful of such cases have been published

Table II - Comparison of the epidemiological, clinical and outcome features of Behçet's disease patients with and without inflammatory optic neuropathy.

	No optic neuropathy group n=420	Optic neuropathy group n=10	p
Mean age (year)	31.4	29	NS
Sex ratio	2.3	2.1	NS
Diagnostic delay (year)	4.2	5	NS
Cutaneous involvement	366 (85%)	8 (80%)	NS
Neurological involvement	121 (28%)	9 (90%)	<0.0001
Ocular involvement	200 (46.5%)	5 (50%)	NS
Blindness	41 (29%)	1 (10%)	NS
Vascular involvement	150 (35%)	1 (10%)	NS
Severity scale (>3)	58 (32.6%)	9 (90%)	<0.0001

NS, not significant.

Table III - Review of published series dealing with optic neuropathy in Behçet's disease.

Study	Akman-Demir et al. (7)	Kidd et al. (8)	SWSW study (9)	Gökçay et al. (16)	Ashjazadeh et al. (10)	Frigui et al. (11)	Our study
No of patients	200	50	22	530	6	376	440
Racial group	Turkish	Mixed	Western European	Turkish	Iranian	Caucasian	Caucasian
Mean F/U duration (months)	42	36	124	Unspecified	65	Unspecified	30
Neurological presentation (%)	3	24	23	10.2	24	27.7	28.8
Optic neuropathy (%)	1	2	9	0.2	0	4.7	2.3

SWSW, South-west of England and south-Wales study; F/U, median follow-up.

(12-20), with one case with histopathology showing gliosis and demyelination within the nerve (12). Pathological features include disseminated softening foci with mild loss of myelin and glial proliferation, perivascular lymphocyte cuffing and variable wallerian degeneration of white matter tracts (1). However, edema and reversible inflammatory damage to the blood-brain barrier have also been advocated to explain complete lesion regression (21).

Cranial MR imaging was pathologic in 5/9 cases. All neuroradiologic findings were related to neurobehçet and no specific lesions of the optic nerve were reported. In no cases was magnetic resonance imaging (MRI) suggestive of optic nerve damage despite abnormal visual evoked potentials. Salvi et al. reported the cases of two women, aged 24 and 37, with inflammatory optic neuropathy inaugurating a BD in which orbital MR imaging showed signal change in the intracanalicular portion of the optic nerve in both cases (15). MR features had a little contribute in establishing the diagnosis. The limited contribution of MR imaging features in terms of differential diagnosis, especially with multiple sclerosis (22, 23), reinforces the view that clinical evaluation is fundamental for the diagnosis of BD.

CONCLUSIONS

Inflammatory involvement of the optic nerve in BD is rare and may happen at an early stage of the disease. But we still think that this involvement is misdiagnosed. According to our experience, an early diagnosis and care of the patient may improve the clinical course. That is why we suggest a systematic investigation by visual evoked potentials in case of neurological involvement and in case of a visual symptom not related to ocular involvement. To our knowledge, this is the largest series of optic neuropathy in BD ever reported.

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