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Clinico-radiological spectrum and outcome in idiopathic hypertrophic pachymeningitis

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ABSTRACT

Objective: To elucidate the clinico-radiological features, treatment response and outcome of a large cohort of patients (n = 20) with idiopathic hypertrophic pachymeningitis (IHP) and to examine if any of these features could differentiate between IHP and secondary causes of hypertrophic pachymeningitis (SHP).
Methods: 20 patients with IHP diagnosed between 1998 and 2009 formed the study cohort. We adopted a validated clinical score to quantitatively assess and document their neurological disability and to compare their pre- and post-treatment outcomes. Appropriate statistical analysis was done to look for any clinical and/or radiological features to differentiate IHP from SHP.
Results: Out of the twenty eight consecutive patients with pachymeningitis, 20 were having IHP and 8 were having SHP (Tuberculosis-5, Sarcoidosis-2, Wegener's granulomatosis-1). In IHP, headache and visual symptoms dominated the clinical symptomatology (80% and 75%). In MRI, the peripheral pattern of contrast enhancement was more common with IHP ($p = 0.03$). The posterior falx and tentorium showing a hypointense center ("fibrosis") and enhancing periphery ("active inflammation") together mimicking "Eiffel-by-night" sign was found to be more commonly associated with IHP (60% vs 12.5%, $p = 0.03$). Biopsy was done in 9 patients. At a mean follow-up of 51 months (range 24–144 months), the mean pretreatment clinical score improved from 6.55 to 1.80 in 20 patients with IHP ($p < 0.001$).
Conclusions: Our data on the largest cohort of patients with IHP would shed light into its clinico-radiological spectrum, treatment and outcome. The prognosis is satisfactory if managed appropriately. We have highlighted the role of MRI in differentiating between IHP and other causes of SHP.

1. Introduction

Hypertrophic pachymeningitis (HP) is characterized by localized or diffuse thickening of the cranial or spinal dura mater which may or may not be associated with inflammation, resulting in progressive neurological deficits [1,2]. It has been described in association with infection, trauma, tumors, and Wegener's granulomatosis [3–5] (Appendix 1). IgG4-related hypertrophic pachymeningitis (IgG4-RHP), a recently described entity, is an increasingly recognized manifestation of IgG4-related disease, a fibroinflammatory condition that can affect virtually any organ. It is estimated that IgG4-RHP may account for a high proportion of cases of hypertrophic pachymeningitis once considered idiopathic [6,7].

From the management point of view, attempts to differentiate primary or idiopathic HP (IHP) from secondary hypertrophic pachymeningitis (SHP) is very important. Definite diagnosis can be obtained after meningeal biopsy, but may not always be possible or warranted. MRI characterizes the degree of dural inflammation and clinches the diagnosis of HP, but till date there is no data on how the imaging helps in differentiating IHP and SHP. Most available literature on IHP being either case reports or small series, focusing on MRI abnormalities or the variable clinical manifestations and the clinical outcome with short follow-up, one cannot deduce any conclusive data on the same. No objective scales assessing the disability have ever been used to quantify the long-term functional outcome of a large group of IHP patients. This is especially important because of the prevailing notion that a majority of these patients do not recover fully and it is a long-standing, chronic disease with remission and relapses.

Therefore, we attempted to elucidate the clinico-radiological and laboratory features, treatment response and outcome of a large cohort of patients with pachymeningitis. We specifically examined if any of these features could distinguish IHP from SHP thus aiding the treating neurologist.

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2. Methods

2.1. Subjects and methodology

This study was conducted at the Sree Chitra Tirunal Institute for Medical Sciences and Technology, a tertiary center for neurological disorders in India. Institutional ethics committee approval was obtained for the study. 28 consecutive patients with hypertrophic pachymeningitis diagnosed between January 1998 and December 2009 were evaluated in detail. We adopted a simple composite clinical score derived from the various clinical manifestations in patients with hypertrophic pachymeningitis available in published literature and then compared the pre- and post-treatment score to evaluate their outcome homogeneously. Each component of the score has been adopted and modified from previously validated clinical scores [8–11]. The details of the clinical scores are provided in Appendix 2a. The authors (GKD and AR) did a detailed chart review to score each of the patient's status at various periods of follow-up, this being a simple scale and the scoring could easily be accomplished in all patients. Each patient was then personally interviewed by the Neurologists (GKD and AR) and patients were also made to score their symptoms before and after treatment in a Likert scale independently (Appendix 2b). The variability if any, in each of the score pertaining to a specific symptom and the composite score as scored by the authors and the patients were statistically analyzed by kappa statistics.

2.2. Investigations

All patients underwent the following investigations: hemogram (hemoglobin, differential and total leukocyte counts, total platelet count), erythrocyte sedimentation rate (ESR), biochemical investigations including serum calcium, phosphorus, liver function tests, renal function tests, serology for human immunodeficiency virus (HIV), rheumatoid factor(RA factor), antinuclear antibodies, APLA (antiphospholipid antibody),serum VDRL (venereal disease reference laboratory testing),P and C antineutrophil cytoplasmic antibodies (cANCA and pANCA) and angiotensin converting enzyme(ACE) assays. Cerebrospinal fluid (CSF) examination was done in all patients for cytology, biochemistry and immunological tests to exclude secondary causes. A Mantoux test was performed in all patients.

2.3. Imaging

Imaging studies included chest X-ray and contrast enhanced MRI brain (1.5 T Scanner, Signa GE, Milwaukee, WI) in all patients. All the MRI scans archived in our system were analyzed by the neuroradiologist (BT) blinded to the clinical data. Follow-up contrast enhanced MRI was performed if clinically indicated, and the findings were classified as (i) improved, (ii) worsened, or (iii) no change in relation to the immediately prior MRI(s). In the final follow-up MRI, the degree of abnormal enhancement was defined as (i) stable when unchanged, (ii) improved when there was less extensive enhancement or reduced thickness of the dura mater, and (iii) worse if there was increased enhancement compared to the initial imaging. [12] The patterns and sites of enhancement were noted and characterized as described by Hatano et al. in 1999 [13]. It was described as linear, nodular and combined. We also classified the pattern of dural enhancement as “peripheral”, “uniform” or “combined”. The involvement of pachymeninges was described as diffuse if more than 2 non-contiguous sites were involved and focal if less than 2 sites were involved and were also subclassified as “symmetric” or “asymmetric” by comparing either side of the brain.

2.4. Brain biopsy

Biopsy was performed in 9 patients and included meninges and/or brain parenchyma. They were stained for infectious agents and cultures were done.

2.5. Statistical analysis

All analyses were performed using SPSS version 17.0 (SPSS Inc., Chicago, IL). Fisher's exact test, Paired *t*-test, kappa statistics, positive and negative predictive values, sensitivity and specificity were applied as appropriate. A p-value ≤ 0.05 was taken as significant.

3. Results

3.1. Clinical profile

Out of 28 patients with HP, 20 patients had IHP and 8 patients had SHP. In the IHP group, there were 11 men and 9 women with a median

Table 1
Clinical features, CSF and MRI findings in patients with hypertrophic pachymeningitis (N = 28).

Characteristics	IHP (N = 20)	SHP (N = 8)	Significance p*
Age, mean, years	49.5	40.8	NS
Sex (female:male)	9:11	5:3	NS
Age at onset of symptoms, mean, years	44.5	39.7	NS
Duration of illness, mean, years	5.1	1.28	NS
Clinical features	N, %	N, %	
Headache	16(80.0)	7(87.5)	NS
Visual symptoms	15(75.0)	3(37.5)	NS
Seizure	6(30.0)	2(25.0)	NS
Hearing loss	4(20.0)	2(25.0)	NS
Dysphagia	3(15.0)	1(12.5)	NS
Dysarthria	2(10.0)	1(12.5)	NS
Ataxia	5(25.0)	2(25.0)	NS
Facial sensory complaints	2(10.0)	1(12.5)	NS
Hemiparesis	2(10.0)	0(0.0)	NS
Quadriparesis	2(10.0)	0(0.0)	NS
Only second cranial nerve involvement	5(25.0)	2(25.0)	NS
Second cranial nerve involvement with other cranial nerve palsies	5(25.0)	1(12.5)	NS
Involvement of oculomotor nerves	7(35.0)	3(37.5)	NS
Facial nerve involvement	2(10.0)	0(0.0)	NS
Eight cranial nerve involvement	4(20.0)	2(25.0)	NS
Bulbar palsy	5(25.0)	3(37.5)	NS
CSF protein, mg% (mean, range)	96.9(30–494)	76(37–159)	NS
CSF glucose, mg% (mean, range)	82(50–154)	82.8(53–153)	NS
CSF cell count (mean, range)	35(2–460)	16(2–75)	NS
Site(s) of involvement in MRI	I		
Falcotentorial	17(85.0)	4(50.0)	NS
Medial frontal	7(35.0)	6(75.0)	NS
Basifrontal	7(35.0)	4(50.0)	NS
Frontal convexity	6(30.0)	5(62.5)	NS
Temporal convexity	6(30.0)	3(37.5)	NS
Skull base	5(25.0)	2(25.0)	NS
Symmetrical involvement in MRI	10(50.0)	4(50.0)	NS
Diffuse involvement	13(65.0)	7(87.5)	NS
Spinal involvement	2(10)	0(0.0)	NS
T2 Signal in MRI			
Hypointense	19(95.0)	6(75.0)	NS
Isointense	1(5.0)	2(25.0)	NS
Peripheral pattern of CE	12(60.0)	1(12.5)	NS
	12(60.0)	1(12.5)	0.03
Follow-up MRI showing improvement	3(15.0)	5(62.5)	0.02

IHP — idiopathic hypertrophic pachymeningitis, SHP — secondary hypertrophic pachymeningitis, N — number, NS — not significant, * — p-value by Fisher's exact test, ^ — see text for description, CE — contrast enhancement.