PREVALENCE OF CEREBRAL AMYLOID ANGIOPATHY (CAA)-RETROSPECTIVE SINGLE CENTRE ANALYSIS FROM 2009 TO 2019

Pathology

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ABSTRACT

OBJECTIVE: The present study aims to analyse the prevalence of Cerebral Amyloid Angiopathy (CAA) among the various neuro surgical tissue samples, to study the histomorphological changes of CAA in neural tissue and to analyse their association with increasing age & neurological disorders.

METHOD: Retrospective analysis and review of all neurosurgical specimens received during the period from 2009 to 2019 was carried out. Review of the clinical details including radiological images, and review of paraffin sections was conducted by two pathologists after appropriate special stains like Congo red.

RESULTS: Among the 301 cases studied, 14(4.65%) had evidence of CAA. Of the 14, 6(42.86%) were males and 8(57.14%) were female All of the 14(10.77%) cases were above the age group of 50 years. In the more than 50 age group, this contributes to 9.68% of males and 11.76% of females.

CONCLUSIONS: CAA is found to be a diagnosis more common in the older age group (>50 years) and with a female preponderance. Familiarising & understanding the pathological sequence and morphological changes of CAA, will help in diagnosis, formulating treatment options for the better clinical outcome of CAA patients

KEYWORDS

Cerebral amyloid angiopathy (CAA), Intra cranial haemorrhage (ICH), Amyloid precursor protein (APP), Alzheimer's disease (AD),

INTRODUCTION:

Cerebral amyloid angiopathy (CAA), is a pathological of deposition of beta amyloid in the walls of small and medium calibre cerebral blood vessels, and associated with aging and variety of neurological disorders like Alzheimer's disease (where there is deposition of beta amyloid as neurofibrils or neuritic plaques), certain types of spongiform leukoencephalopathies etc¹. CAA is frequently sporadic, although genetic and familial forms exists due to point mutations of genes encoding beta amyloid peptide and persons with ApoE4 genotype². Morphological changes in neuroparenchma includes micro hemorrhages, micro infarcts, sub cortical white matter changes, leukoencephalopathy, superficial siderosis (as seen in MRI), and most importantly the clinically significant intra cerebral hemorrhages that calls for neurosurgical procedures that is lifesaving. CAA induced hemorrhages are superficial lobar, where as in hypertensive hemorrhages they are in deep bulbar or ganglionic region³. Cerebral vessels in CAA shows variety of morphological changes that include "double barrelling" caused by circumferential cleft, thickened vessel wall, occasional intramural lymphocytic infiltration(FIGURE 3), less frequently as vasculitis if necrotising or granulomatous type. Patients show signs and symptoms related to anatomical location and size of haemorrhage, like head ache, vomiting, dementia, transient neurological events, and coma. Management of patients by multidisciplinary team including neuro-surgeons, neuro-physicians, radiologists, pathologists etc., has a better clinical outcome.

MATERIALS AND METHODS:

Neuro-surgical operative specimens obtained by procedures like evacuated blood clot in case of ICH, brain tissue for neoplastic and non- neoplastic conditions from patients of all age group and gender were included in this study period from 2009 to 2019. Clinical data and pathological slides were reviewed with re-staining with Hematoxylin & Eosin, Congo-red stain for light and polarising microscopy. Immuno-histochemical procedures was not included in this study.

INCLUSION CRITERIA;

All neuro-surgical specimens like brain biopsy for neoplastic and non-neoplastic lesions, evacuated tissues for ICH etc., were included irrespective of age and gender.

EXCLUSION CRITERIA:

Samples containing only blood clot and inadequate brain tissue with sparse parenchyma and blood vessels were excluded from this study.

RESULTS:

S. No	Pathological specimen	Age group			Gender		Total
		< 14 years	15 – 50 years	>50 years	Male	Female	
1	Evacuated ICH	10	22	46	37	41	78
2	Evacuated SDH&EDH	12	53	62	72	55	127
3	Neoplastic	21	39	16	28	48	76
4	Non-neoplastic	2	12	6	8	12	20
Total		45	126	130	145	156	301

DISCUSSION:

Definite Cerebral amyloid angiopathy is a pathological diagnosis, yet there are several international guidelines like "The Boston CAA Group"⁴, providing four levels of certainty in the diagnosis of CAA based on autopsy, brain biopsy and imaging techniques namely,

1. Definite
2. Probable
3. Probable
4. Possible

In the present era of decreasing frequency of clinical or pathological autopsies, evaluation for CAA from any amount brain biopsies taken for other indications shall be of great benefit for the clinicians & patients in form of better clinical outcome. Brain biopsy has a sensitivity of 53% & a negative predictive value of 70% for the diagnosis of CAA.⁶

The CAA is one of the major causes of atraumatic superficial lobar intra cranial haemorrhage (ICH).⁷ Hypertensive bleeds are frequently seen in the deep ganglionic or bulbar regions.⁸ In the present study five such samples were received, but excluded due to absence brain tissue.

The present study shows evidence of CAA in 4.65% and 9.68% in men aged more than 50 years and 11.76% in women aged more than 50 years suggesting a female preponderance. This is comparable to

autopsy series finding evidence of CAA in 18.3% & 28% of men and women aged more than 50 years respectively.⁹

In a series of 117 brain biopsy samples of patients with confirmed Alzheimer's disease, 83% had evidence of CAA.¹⁰ The present study had one patient aged 78 with confirmed Alzheimer's disease with features of CAA.

Recurrent intra cranial haemorrhage was noticed in 14.2% of the confirmed cases of CAA, compared to published series with 25-40% recurrences and 36% such recurrences occurring in the same location.¹¹ Combined clinical, radiological, biochemical and pathological techniques increases the sensitivity and specificity for the diagnosis of CAA.¹² Treatment with steroids is considered for CAA related inflammation.¹³

CONCLUSION:

The present study shows evidence of CAA associated with increasing age with all samples found in the age group of > 50 years. A female predominance (male 42.86%, female 57.14%) was noted. Recurrent ICH was found in 14.2%. Familiarising & understanding the pathological sequence and morphological changes of CAA, will help in diagnosis, formulating treatment options for the better clinical outcome of CAA patients. Relevant anti-hypertensive, anti-platelet and anti-coagulant treatments may be formulated in appropriate settings. Avoiding any degree of head injury and life style modifications may be advised, although routine activities need no restriction.

Figure 1: Evacuated black hemorrhagic and white solid brain tissue fixed in buffered formalin.

Figure 2: Black hemorrhagic and solid white post fixed brain tissue in buffered formalin.

Figure 3: Microscopic picture of cortical tissue containing blood vessels, 10X magnification.

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