Are alpha-1-antichymotrypsin and inter-alpha-trypsin inhibitor peripheral markers of Alzheimer's disease?

The definite diagnosis of Alzheimer's disease (AD) requires both clinical criteria of probable AD and neuropathological evidence of AD lesions. At present there is no laboratory test for a pretreatment diagnosis. Recently, genetic and histochemical studies identified protease inhibitors as components that might be implicated in the formation of the amyloid substance in AD brains. First, Abraham et al. suggested a potential role of alpha-1-antichymotrypsin (ACT) in the pathogenesis of the lesions, moreover Matsubara et al. found an increased serum concentration of ACT in AD. Second, several authors showed that one transcript of A4 amyloid precursor contained an additional sequence similar to the active site of inter-alpha-trypsin inhibitor (ITI). The purpose of our study was to test the diagnostic value of ACT and ITI in serum and CSF from AD patients.

Sera and CSF were collected from eight men and 16 women with probable AD, mean (SD) age 66 (9) years, and from a control group of 19 men and six women aged 64 (8) years. Controls were volunteers free of any neurological disease, with a MMS score higher than 28, who had had a myelo or radiculography for proven disk herniation. CSF was not collected especially for this study. The procedure was approved by the ethical committee of Lille. ACT and ITI contents were measured by electroimmuno-diffusion methods. Semi-quantitative determination was used for ITI in CSF because of its low concentration. Statistical assessment used non parametric tests (Mann and Whitney's U test and Spearman's rank correlation test).

In the control subjects there were 1) no difference in serum or CSF ACT and ITI contents between males and females, 2) no correlation between age and both serum ITI and CSF contents, 3) a positive correlation between serum ACT contents and age (p < 0.02).

Between AD patients and controls, there were no difference in serum or CSF ACT and ITI contents, and no difference of the ACT/CSF ratio (table).

In our patients there was no correlation between the severity of dementia on MMS and Blessed scores and serum or CSF ACT contents, and a negative correlation between MMS and Blessed B scores and serum ITI contents (p < 0.05).

Our results show that ACT and ITI are not useful markers of AD in serum and CSF. They don't confirm that of Matsubara et al. The ACT CSF/serum ratio was not significantly modified in AD patients, which is consistent with the hypothesis that the blood-brain barrier is not strongly affected in this disease. The correlation between serum ITI contents and the severity of the dementia could be explained by non specific metabolic disturbances.

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Postradiation motor neuron syndrome of the upper cervical region—a manifestation of the combined effect of cranial irradiation and intrathecal chemotherapy?

CNS prophylaxis is now an integral part of the treatment of acute leukaemia and lymphoma to report an unusual case of neurogenic amyotrophy apparently resulting from damage to the anterior horn cells of the upper cervical cord and lower brainstem during cranial irradiation.

The patient presented at the age of 13 in January 1977 with T-cell acute lymphoblastic leukaemia and was treated according to the United Kingdom Acute Lymphoblastic Leukaemia Trial 4 (UKALL 4) (intensive) schedule. This comprised induction with cyclophosphamide, cytosine arabinoside (ara-C), vincristine, prednisolone and intrathecal ara-C, with the same, together with adriamycin, asparaginase, 6-mercaptopurine, intrathecal metomethoxate and cranial irradiation; and maintenance with vincristine, metomethoxate, ara-C, 6-mercaptopurine and prednisolone. The total dose of irradiation was 2400 cGy (rads) and the field extended to the level of the C3 vertebral body.

Apart from an early bone marrow relapse in June 1977, he made a complete clinical recovery. In particular, there was no evidence of CNS involvement at any time.

He received his last dose of vincristine in May 1979 and completed his chemotherapy by June 1979. The period of cranial irradiation spanned 19 days in April 1977.

In January 1981 he was referred to the neurology clinic with a three month history of progressive painless wasting and weakness of the shoulder girdle muscles. There was marked bilateral wasting of the scapulae, left worse than right. The trapezi, rhombohoids, supra- and infraspinati, deltoids, teres major and both sternocostal and clavicular heads of the pectoralis major muscles were wasted, more on the left, and power was reduced to grade 4 on the left and 4 + on the right. There was minimal weakness of the biceps, triceps and infraspinati; deltoids were spared as were the distal upper limb muscles and lower limbs. There was questionable weakness of the orbicularis oculi and failure of frontalis to maintain elevation of the eyelids. Although his face was thin there was no focal wasting or demonstrable weakness of the other facial muscles. There were no sensory symptoms or signs. Tendon reflexes were well preserved and symmetrical. Plantar responses were flexor.

Investigations at this stage including muscle enzymes, thyroid function, cervical spine radiographs, haematological screen and bone marrow were normal. Electromyographic (EMG) studies revealed reduced amplitude ulnar sensory nerve action potentials and evidence of chronic partial demyelination of both deltoids, more on the left.

After the condition appeared to arrest with no objective progression noted during eight years of follow up (1981–9), serial EMGs showed evidence of chronic partial denervation and reinnervation in the brachioradialis, biceps, deltoids, supraspinatus and trapezius muscles without pathological activity at rest. No significant abnormality was demonstrated in the lower limbs.

In the right tibialis anterior a full interference pattern contained occasional polyphasic units of normal amplitude and duration which were not felt to be of clinical significance. Muscles

Table Alphabetical antichymotrypsin (ACT) and Inter-alpha-trypsin inhibitor (ITI) contents, CSF ACT contents and ACT/CSF ratio in controls and Alzheimer's disease (AD) patients.

<table>
<thead>
<tr>
<th>Controls Group</th>
<th>ACT Patients</th>
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<tbody>
<tr>
<td>Serum</td>
<td>0.67 (0.27) g/l</td>
</tr>
<tr>
<td>CSF</td>
<td>0.63 (0.22) g/l</td>
</tr>
<tr>
<td>Serum/CSF</td>
<td>11.0 (4.5)</td>
</tr>
<tr>
<td>Serum</td>
<td>0.71 (0.19) g/l</td>
</tr>
<tr>
<td>ITI mean (SD)</td>
<td>0.72 (0.29) g/l</td>
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</table>

ACT, ACh, tauit, and men pheral the diagnostic higher non histochemical genetic age (SD) in lesions, the an kidney's definite The test). The serum was the contents, the committee ethical (AD) requires (AD) in AD. Moreover, the inhibitor are implicated in Alzheimer's disease: Report of the NINCDS-ADRDA work group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 1984;43:939-44.


Optic nerve cysticercosis: a case report

Cysticercosis is caused by infection from the larval form of *Taenia solium* and humans are an intermediate host. The subcutaneous tissue, brain, eye, muscle, heart, liver and peritoneum are common sites of encystment.1 In the eye, the conjunctiva is the most common site. Subretinal and intraretinal locations have also been described.2 Cysticercosis of the intracranial portion of the optic nerve is rare. A 15 year old school girl presented with deteriorating vision in her right eye which had progressed over a seven month period. There was no history of pain or inflammation in the eye, trauma, headache, vomiting, seizures, or subacute or chronic physical and systemic examinations were normal. There was no subcutaneous nodule or cafe-au-lait spots. Neurological examination was also normal except for the patient's inability to count fingers at less than 30 cm with the right eye. The pupils were equal and reacting. Fundus ocular examination revealed disc pallor in the upper half, disc margins elevated in the lower half, and the neighboring retina for an area of two dioptries below the disc. Vessels and macula were normal. Pigmentary changes were present. The tension was 17.3 mm in both eyes. Other cranial nerves were normal. The results of the neurological examination did not reveal any abnormality.

Optic nerve involvement is rare in any kind of cyst or granuloma. As a result, in our study, no cases of optic nerve involvement were encountered.

Haematological and biochemical parameters were normal. The erythrocyte sedimentation rate (ESR) was 26 mm and the VDRL was negative. Skull radiographs of the optic foramen and superior orbital fissures were normal. CT scan of the head and orbit with contrast enhancement showed a retrolubar segment of the right optic nerve thickened with a small area of low attenuation in the thickened portion of the optic nerve. Retrolubar fat was preserved and the muscle cone was normal. The optic nerve at the orbital apex appeared to be of normal width. The brain parenchyma was normal as was the left optic nerve (fig). Perimetry revealed superior altitudinal right hemianopia. Ultrasonography showed a mass in the region of the right optic nerve. The Casoni test was negative.

A diagnosis of optic nerve glioma or granuloma was considered. A right front cranio-tomy and extradural frontal orbitotomy was performed. After incising the tenon's fascia normal retrolubar fat protruded. The optic nerve was exposed by microdissection and was found to have fusiform thickening. A small portion of nerve just behind the optic globe was normal as was nerve near the apex of the field. Incision in the maxillary sinus was made over the maximum bule. There was intense fibrosis. On deeper incision a sago grain like cyst was found and excised. Histopathology revealed it to be cysticercosis. Postoperatively the patient's vision fully recovered but there was III r nerve paresis.

Cysticercosis is one of the most serious public health problems in the developing countries.1 Any part of the neuraxis can be involved, except the peripheral nerves, resulting in protein features.2 Ocular cysticercosis occurs in 3% of cases and may be single, unilateral or bilateral.3 Subretinal involvement of the eye usually occurs initially through the posterior ciliary arteries but migration of the parasite is common. The nasal side of the eye is more commonly involved than the lateral side. This is due to an anatomical peculiarity of the ophthalmic artery which after giving rise the lacrimal branch runs along the medial side of the orbit and divides into its terminal branches.4 The optic nerve obtains its blood supply from the branch of the central artery of the retina and retinal blood vessels may thus be involved. The usual symptoms are of pain, irritation of the eyes due to iodocyclitis and dimness of vision. The eye may be involved alone or may be associated with other clinical features of neuro-cysticercosis when the brain is also involved.

Optic nerve involvement is rare in any kind of cyst or granuloma. As a result, in our study, no cases of optic nerve involvement were encountered.