patients in central and north Europe,\textsuperscript{1,2} while an analogous evidence is lacking in Italian,\textsuperscript{3} and Israeli patients.\textsuperscript{4} Such an association between HLA-A\textsubscript{3} and B\textsubscript{1} antigens and multiple sclerosis also has not been proven in Japanese\textsuperscript{5} and Indians.\textsuperscript{6}

In view of the unique immunogenetic profile of the Greek population\textsuperscript{7} we studied the HLA A and B specificities in 81 Greek patients with a well established diagnosis of multiple sclerosis. Fifty specific antisera were used, determining 24 HLA A and B antigens (9 and 15 respectively) according to the standard microlymphocytotoxicity test.

The results were compared to those of 280 healthy unrelated controls. For statistical evaluation, the $X^2$ analysis was applied after Yates correction and multiplication of the $p$ values by the number of antigens tested (P corrected). As it can be seen, (table) the frequency of HLA A\textsubscript{3} and B\textsubscript{1} antigens in the patients group (44-4\% and 33-3\% respectively) was significantly greater than that in the controls (26-0\% and 13-21\% respectively). The relative risks (RR) for the antigens A\textsubscript{3} and B\textsubscript{1} were 2.23 and 3.23 respectively. Our results thus show that Greeks, unlike Caucasian ethnic groups of the Mediterranean area, there is an increased frequency of HLA A\textsubscript{3} and B\textsubscript{1} antigens in multiple sclerosis patients, analogous to that observed in populations of central and northern Europe. We think that this observation, should be reported, as contributing to understanding of the complex immunogenetic profile of this disorder.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|}
\hline
Antigens & Controls (280) & Patients (81) \\
& \textbf{no} & \textbf{no} \\
\hline
HLA-A\textsubscript{3} & 71 (25,35) & 20 (24,4) \\
A\textsubscript{2} & 150 (53,57) & 41 (50) \\
A\textsubscript{1} & 73 (26,07) & 36 (44,4) \\
A\textsubscript{4} & 100 (35,71) & 24 (29) \\
A\textsubscript{6} & 36 (12,85) & 10 (12) \\
A\textsubscript{11} & 27 (9,64) & 15 (18,3) \\
A\textsubscript{8} & 26 (9,28) & 2 (2,4) \\
A\textsubscript{14} & 18/226 (7,96) & 3 (3,7) \\
A\textsubscript{16} & 11/226 (4,86) & 2 (2,4) \\
\hline
HLA-B\textsubscript{1} & 91 (32,5) & 30 (36,6) \\
B\textsubscript{1} & 37 (13,21) & 27 (33,3) \\
B\textsubscript{3} & 35 (12,50) & 10 (12,0) \\
B\textsubscript{2} & 51 (18,21) & 16 (19,5) \\
B\textsubscript{3} & 29 (10,35) & 6 (7,3) \\
B\textsubscript{4} & 22 (7,85) & 7 (8,5) \\
B\textsubscript{5} & 22 (7,85) & 5 (6,2) \\
B\textsubscript{6} & 10/212 (4,71) & 2 (2,4) \\
B\textsubscript{7} & 24 (8,57) & 6 (7,3) \\
B\textsubscript{8} & 8,3 (29,64) & 25 (30,8) \\
B\textsubscript{12} & 11/231 (4,76) & 1 (1,2) \\
B\textsubscript{17} & 18 (6,42) & 2 (2,4) \\
B\textsubscript{18} & 59 (21,07) & 8 (9,7) \\
B\textsubscript{35} & 17/226 (7,52) & 6 (7,3) \\
\hline
\end{tabular}
\end{table}

\textsuperscript{2}RR 2.23 $X^2 = 10.46$ P corrected 0.001
\textsuperscript{3}RR 3.33 $X^2 = 24.83$ P corrected 0.001

References


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Papilloedema with extramedullary erythropoiesis and Cushing's syndrome

Sir: Extramedullary erythropoiesis may cause a variety of clinical problems depending on the site or sites at which it occurs. Various locations are well recognised by central nervous system involvement, although documented, is relatively uncommon. We describe a case where there was cranial involvement presenting in a very unusual fashion, the clinical features arising because of the particular location of the erythropoietic tissue in the pituitary fossa, in a patient who concomitantly and coincidentally had a pituitary adenoma.

A 55-year-old Greek Cypriot lady presented in 1977 with a fracture of her humerus following a fall. A blood count showed her to be anaemic. On direct questioning she gave a history of listlessness for at least six years and a family history of anaemia. Examination revealed a moderately enlarged spleen, first noted at the age of 10 years. Investigations showed haemoglobin 8.4 g/dl; red cell appearances of thalassemia intermedia; starch gel electrophoresis showed mainly HbA with HbA\textsubscript{2} 6.4\% and HbF 8.6\%, confirming the diagnosis of beta thalassemia intermedia. Routine chest radiographs showed a posterior mediastinal mass which proved to be extramedullary erythropoiesis on $^{57}$Fe scanning. This also demonstrated increased uptake by the spine, pelvis and liver.

In 1980 her face became puffy and her changed appearance clinically suggested Cushing's syndrome. This was confirmed by the following investigations: 9.00 am cortisol 755 nmol/l; midnight cortisol 775 nmol/l; 9.00 am cortisol following 1 mg dexamethasone at 11 pm, 945 nmol/l; urinary free cortisol 6485 nmol/l; 24 hr plasma ACTH 17 ng/l. Her plasma prolactin was above 5000 mU/l on three occasions. It was noted from her history that she had no children and had had secondary amenorrhoea since the age of 33, but had no galactorrhoea.

Skull radiographs showed erosion of the posterior clinoid processes, but computed tomography did not show expansion of the sella turcica or any abnormality in the pituitary fossa. At this stage she was considerably disabled by a proximal myopathy.
and severe osteoporosis with four vertebral crush fractures. She was also severely depressed. She was treated at this stage with metyrapone 1500 mg daily, and regularly transfused in an attempt to reduce extramedullary erythropoiesis and improve the state of her bones. Three weeks later she developed severe frontal headaches, bitemporal hemianopia to red, papilloedema and fundal haemorrhages. A clinical diagnosis of haemorrhage into a pituitary tumour was made. She had reduced white cell and platelet counts because of hypersplenism. There was no evidence that metyrapone had exacerbated her haematological problems. A transethmoidal hypophysectomy was therefore performed as an emergency. The floor of the pituitary fossa was found to be thinned and deficient in area. Extradurally, greyish-red tissue was noted and found on frozen section to be erythropoietic tissue. This “tumour” almost filled the fossa, but after its removal the dura around the pituitary was identified and opened. Frozen section biopsy and subsequent histology showed a mixed acidophilic and basophilic adenoma involving the whole of the anterior pituitary. The patient made a satisfactory recovery and her Cushingoid features have largely regressed. The papilloedema and haemorrhages have resolved. She subsequently underwent splenectomy for her hypersplenism.

Extramedullary erythropoiesis occurs in a variety of haematological conditions and is well recognised in beta thalassemia intermedia.1 Sites most commonly involved are spleen, liver, lymph nodes, gastrointestinal tract, kidneys and lungs, but a variety of sites have been reported including the dura mater, more usually involving the nasal dura mater.2-4 However, cranial dura mater involvement is also recognised, and in one recent report extramedullary haemopoiesis in the cerebral meninges was thought to be the probable cause of papilloedema and visual field defects.5 In that case, however, the cranial dura was found to be heavily involved at necropsy, and the falx cerebri was thickened. There was also cerebral oedema.

In our patient there was no evidence on computed tomography of extensive dural involvement, hydrocephalus or cerebral oedema. The most likely explanation for the acute papilloedema was rapid chiasmal compression by expansion of the extradural erythropoietic tissue in the pituitary fossa. The erythropoietic tissue was entirely extradural and a transcranial surgical approach might have missed the true cause of the chiasmal compression. The fact that the fundal changes resolved post-operatively suggests that the papilloedema was caused by the particular site rather than the extent of the lesion.

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