Letters to the Editors

Antipituitary antibodies in patients with pituitary abnormalities and hormonal deficiency

Sirs, Mau et al. (1993) reported the results of antipituitary hormone autoantibodies (APHA) in adult patients, six with primary empty sella syndrome (ESS) and five with pituitary tumours identified by magnetic resonance (MR) imaging or computed tomography scan, compared to those of six normal volunteers. Five patients (45%), two with ESS and three with pituitary tumour, had positive APHA which did not correlate with the type of hormonal deficiency present, indicating that they are neither specific nor predictive.

We studied 43 hypopituitary patients (29 male and 16 female) aged 3-22 years (mean age 12.4±4.0 years) and determined pituitary antibodies by indirect immunofluorescence on unfixed cryostat sections of monkey pituitary. All were examined by MR (Maghnic et al., 1991) which revealed anterior pituitary abnormalities in 34 of them. In particular, 22 (group I, mean age 14.3±4.9 years) had anterior pituitary hypoplasia, invisible pituitary stalk and ectopic posterior pituitary, nine with isolated GH deficiency (IGHD) and 13 with multiple pituitary hormone deficiency. Twelve (group II, mean age 9.9±2.8 years) had isolated anterior pituitary hypoplasia and IGHD. Eleven (group III, mean age 12.2±1.4 years) had normal morphology of pituitary gland and IGHD. The period of GH treatment before antipituitary antibodies evaluation was 0-2-9 years (mean 5.8±3.4 years) in group I, 0-2-7-2 years (mean 2.7±2.6 years) in group II and 1-2-6-9 years (mean 2.4±1.6 years) in group III. In two patients of group II, the evaluation was made at diagnosis of GH deficiency before the beginning of GH treatment.

Antipituitary antibodies were positive in one girl with normal karyotype, normal pituitary gland morphology and IGHD, and remain so 2 years after the first evaluation; the significance of this is still to be clarified. They were negative in all the others as well as in 20 normal controls. Bottazzo et al. (1980) described a girl with Turner’s syndrome, GH deficiency and GH cell antibodies in which no radiological examination was undertaken. In the study by Mau et al. (1993), APHA were positive in 33% of the patients with ESS while antipituitary antibodies were positive in 75% of the patients studied by Komatsu et al. (1988) who suggest that pituitary atrophy in ESS may be a result of an autoimmune process. Since the autoantibodies were negative in the controls of both studies, the frequency of APHA of 33% in ESS by Mau et al. (1993) should not be underestimated and in our opinion could serve as markers of pituitary diseases in the adults, even though they are not specific. To find the real meaning, however, in terms of physiopathology and mechanisms requires more investigation.

In our study antipituitary antibodies were negative in the presence of pituitary abnormalities. In particular, in children with pituitary insufficiency, empty sella (ES) is considered an epiphenomenon of anterior pituitary hypoplasia (Maghnic et al., 1990); the absence of antipituitary antibodies strengthens the hypothesis that ES in children may be an entity distinct from that in adults. We are aware that different non-standardized methodologies with different substrate (human or animal) for evaluating antipituitary antibodies may give non-comparable results. Nevertheless, no temporal relationship between the times of examination and pituitary antibody results were found. In a few patients, including the positive girl, antipituitary antibodies remained negative several years after the first evaluation. Thus, pituitary hypoplasia in our patients seems unlikely to be secondary to an autoimmune process as observed in adults, indicating that its aetiology is different in children. This suggests that at least in the first two decades screening for antipituitary antibodies is not necessary in the presence of hormonal deficiency and pituitary abnormalities.

The discrepancies in the conclusions drawn by Komatsu et al. (1988) and Mau et al. (1993) could result from the differences of sex and age as well as of race of the patients studied. Indeed, autoimmune processes (or autoantibodies) are more frequent in females and in the elderly. While the patients of Komatsu et al. (1988) were mostly women (82%) and older (73% > 50 years), those of Mau et al. (1993) were prevalently males (83%) and younger (50% < 50 years), probably explaining the low frequency of APHA observed by the latter in ESS.

Mohamad Maghnic
Renata Lorini
Francesca Severi
Department of Pediatrics, IRCCS Policlinico S. Matteo, University of Pavia, Pavia, Italy

References


Sirs, Maghnin, Lorini and Severi present data on 45 paediatric patients with hypopituitarism in whom antipituitary antibodies were negative in all but one. This certainly conforms to data we presented in *Clinical Endocrinology* (Mau et al., 1993). Several distinct differences between Maghnin’s population and ours require elucidation. Our pituitary patients were all adults, presenting with abnormal imaging studies of the sella turcica with or without hormonal abnormalities. Maghnin’s population was a paediatric age group presenting with hormonal insufficiency and had anatomic abnormalities by imaging in only 75% (34 of 45) cases. Clearly, the etiology of pituitary disease in the paediatric age group includes congenital developmental abnormalities whereas in our adult population it would be entirely acquired defects. Nonetheless, Maghnin’s data confirm the lack of immunologic markers to pituitary disease in yet another patient population.

We agree with Maghnin that continued investigation of antipituitary antibodies is valuable in the evaluation of presumptive pituitary disease. We have utilized such antibody testing as a diagnostic tool in the evaluation of lymphocytic hypophysitis. The probable autoimmune nature of this disorder makes the application of antipituitary antibodies more useful and probably more discriminating (Bevan et al., 1992; Mau et al., 1994). Caution must be exercised, however, as cases of lymphocytic hypophysitis without measurable antipituitary antibodies have been described (Guay et al., 1987). In Cosman’s review of lymphocytic hypophysitis, five cases were examined for the presence of antipituitary antibodies and only two of those five were found to have antibodies present (Cosman et al., 1989).

Sensitivity and specificity assessment of antipituitary antibodies is critically important as evidence exists for the formation of non-specific pituitary antibodies in response to viral infection (Yoon et al., 1992). Molecular mimicry between rubella virus and pituitary cellular epitopes other than the hormone product have been noted. The lack of passive transfer of lymphocytic hypophysitis following injection of these antibodies argues against the causative nature of the antibody response.

Clearly, additional investigation is necessary to (1) standardize laboratory techniques for the quantitative or semi-quantitative assessment of antipituitary antibodies, (2) elucidate cellular epitopes other than the hormone product, and (3) evaluate sensitivity and specificity of such assays in patients with a wide variety of known pituitary disease in large-scale studies.

R. E. Ratner
M. K. Mau
T. M. Phillips
George Washington University School of Medicine
Endocrine Division and Department of Immunochromy
Washington, USA

**References**


