Journal of Chromatography, 579 (1992) 187–188
Biomedical Applications
Elsevier Science Publishers B.V., Amsterdam

CHROMBIO. 6416

Discussion

Sensitivity and specificity of urinary N-acetyldopamine as a marker for neuroblastomas: comparison with traditional urinary catecholamine metabolites

Reply to Muskiet and Kema

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(Received April 21st, 1992)

We have carefully studied Muskiet and Kema's comments on our paper and wish to reply as follows.

We consider that our study of 39 neuroblastomas (abdominal and thoracic), 8 nephroblastomas and other tumours such as Askin's tumour, Pepper syndrome, etc., shows that non-secreting neuroblastomas exist [1–4] and are more likely to be thoracic neuroblastomas.

We do not believe that N-acetyldopamine (NADA) testing produces false-positive results in the diagnosis of "classically" functioning neuroblastomas. Among others, we have an example of a 9-year-old child with an abdomino-thoracid neuroblastoma. Whilst the levels of free NADA increased 16-fold above normal levels in this child, total NADA 26-fold, noradrenaline (NA) and adrenaline (A) 25-fold, vanylmandelic (VMA) 8-fold, normetanephrine (NMA) 84-fold, L-dihydroxyphenylalanine (L-Dopa) 50-fold and vanillic acid 20-fold, only the levels of homovanillic acid (HVA) and dopamine (DA) were normal. Thus there was no misdiagnosis: the results of testing NADA were very positive, as were those for the other catecholamines.

We agree with Muskiet and Kema on the value of testing free dopamine. Indeed, we could quote two cases of children who had a total remission for several years. During that period repeated testing of the above-mentioned catecholamines showed all levels to be normal except for free dopamine, which remained elevated until a fatal recurrence. We chose not to give the results of the testing of free dopamine as this was not the object of our study. A comparison of our results will be published later. Moreover, we have noticed that the levels of free dopamine remained normal in cases of nephroblastoma. It is the level of free HVA which is measured classically and not total HVA after enzymatic hydrolysis.

To answer the comment concerning 3-methoxy-4-hydroxyphenlylpyruvic (VPA), which is

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0378-4347/92/$05.00

the precursor of VLA, we would refer readers to our paper [5] (reference 33 in the original paper), where we give a simple diagram of the metabolism of catecholamines. We did not give the values of NADA by age, as we normally do, because the values were very low and there was no ambiguity in cases of neuroblastomas, where the values were 10–50 times higher. It is certain that the determination of urinary NADA and VLA is very delicate and requires sensitive handling. One must also control very closely the parameters that can enhance sensitivity and specificity in order to avoid all interferences.

Attention must be paid to any testing that can make a contribution to the as yet poorly elucidated problem of non-secreting neuroblastomas. For this reason we believe that attention must be paid to NADA, the more so because various N-acetylated amines have also been detected in the urine of patients with neuroblastomas, pheochromocytomas and carcinoid tumours [6].

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