Alcaptonuria with Seizures

Sir: Alcaptonuria, an inherited metabolic disorder of tyrosine metabolism presents in childhood without any symptoms other than the complaint of darkening of urine on standing. We wish to report the occurrence of seizures in one of our cases of alcaptonuria.

An 8-year-old school boy (A) with normal birth history and normal developmental milestones presented with occasional seizures. The first fits of generalised tonic-clonic type occurred on the 4th day of life and thereafter attacks occurred approximately once a year. A casual mention was made by his parents that his urine became dark on standing and his undergarments were stained, so alcaptonuria was suspected. There were no symptoms of joint pain or back-ache. His intelligence was normal. Neurological examination revealed no abnormality and clinical, radiological and ECG examination of the heart were non-contributory. On enquiring into the family history, it was found that he had four sisters and a brother. His 23-year-old eldest sister (AL) had also a similar darkening of her urine on standing, and darkish triangular pigmentation was seen in the sclerae of her eyes. Neither she nor the other sibs had convulsions or joint pains.

Routine investigations, including total and differential WBC counts, haemoglobin content, ESR, blood sugar, urea and cholesterol were normal in both A and AL. CT head scan revealed no abnormality in A. The urine of both the sibs showed no albumin, sugar or deposits on preliminary examination but did turn darkish brown on standing. The presence of homogentisic acid in the urine of A and AL was proved by paper chromatography. The EEG in both cases showed evidence for epileptic activity. There were clear-cut bilaterally synchronous 3 to 3½ Hz high voltage slow wave bursts appearing rhythmically, with independent discrete and synchronous spike discharges over both hemispheres in the EEG of the boy; the EEG of the asymptomatic sister also showed evidence of epileptic activity in the form of bilaterally synchronous spike discharges. The EEGs of the other sibs were normal.

The presence of alcaptonuria and seizures in two cases described may be a fortuitous coexistence. However, only the two sibs (out of the six) who had alcaptonuria had epileptic discharges on the EEG, with one of them (A) also manifesting overt convulsions. No one else suffered from seizures in the family and the EEGs of the sibs with no alcaptonuria were normal. The association of seizures with certain types of disordered amino acid metabolism is well known. The commonest situation is probably phenylketonuria, where EEG changes have been studied in detail. It is hypothesised that damage to the brain occurs very early in life when the immature brain is presented with abnormal patterns of amino acids from which it cannot construct its essential and permanent components. Cases of alcaptonuria picked up occasionally nowadays are not reported in the literature unless some remarkable or strange clinical features are present. In addition to the well known scleral pigmentation and ochronotic arthropathy that are the hallmarks of the full classical clinical presentation, a few rare features also have been reported. They include heart disease, prostatitis, renal stones, and "nephrosis." So far, no case of alcaptonuria has been described with seizures; and this prompted us to report this association of alcaptonuria with seizures although the exact mechanism remains unclear.

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