A 66-year-old man was admitted to our Department for a sudden loss of consciousness, tonic–clonic movement and psychomotor agitation. During the previous 4 months the patient had complained of drowsiness, fatigue, lack of appetite, and nausea. During the prior 2 months he had experienced hair loss, coating of the tongue, and skin flaking with pruritus.

Two hours prior to admission, the patient had experienced loss of spacio-temporal orientation, dizziness, cold sweats, postural instability, and sudden loss of muscle tone in the lower limbs causing a collapse on the ground.

On physical examination the skin was dry, greyish, markedly flaky; and the tongue was pale. There was a circumoral dermatitis, as well as a skin rash described as scaly (seborrhoic) and red (eczematous) distributed around the eyes, nose and mouth, along with alopecia and thinning hair. The vital signs were: rate 75 beats/min, blood pressure 145/90 mmHg, and normal respirations.

The social history revealed that during the previous year the patient had established a chicken farm, and that each morning, when he had gone to collect the newly laid eggs, he had ingested some of the eggs whose shell was broken. For 3 months, he had eaten daily a mean 6 g of albumen.

Laboratory evaluation revealed a minor elevation of the serum cholesterol level. Complete blood count, thyroxine, vitamin B12 and folic acid levels were within reference range. Computerized tomography and magnetic resonance imagining of the brain and spinal cord were normal. No lesions were observed in the temporo-mandibular joint.

The audiometric, vestibular and tilt-test examinations, together with electronystagmogram, electroencephalography, electrocardiogram (ECG) and carotid Doppler studies were unrevealing.

Additional investigations ruled out infective and autoimmune causes, as well as malignancies.

Because of the inability to reach a diagnosis, despite the use of sophisticated technologies, we decided to investigate and review the history of the patient.

Much to our surprise, we discovered that at admission, the laboratory determination of biotin was low (98 pmol/L), confirming the diagnosis of egg white injury syndrome (Table 1).

Although data are lacking to effectively guide the frequency of follow-up and the specific testing warranted, a reasonable strategy is to follow a patient and re-evaluate him, after biotin supplementation for 1 month, including measurement of biotin status. Our patient was treated with 5 mg for 1 month of diathynil neobiotin. Neurologic signs disappeared after 24 h, and the skin lesions after 10 days.

The patient has been followed up monthly for 6 months, without clinical and serum alterations.

Neurologic and cutaneous manifestations are related to “egg white injury”, a cause of biotin deficiency.

Biotin (also called vitamin H or coenzyme R) is a water-soluble vitamin of the B complex. “H” is the initial of “haut”, the German word for skin, because of the skin involvement in deficiency states [1].

The mechanism by which ingestion of raw egg whites leads to biotin deficiency is the irreversible binding of biotin by avidin, a glyco-protein present in the albumen of raw eggs. The resulting compound renders this vitamin non-absorbable by the human gastro-intestinal tract [2]. Cooking denatures avidin, rendering it susceptible to
Table 1 Serum parameters levels in our case, compared with normal range

<table>
<thead>
<tr>
<th></th>
<th>Normal range</th>
<th>Our patient at admission</th>
<th>After 1 week of biotin supplementation</th>
<th>After 1 month of biotin supplementation</th>
<th>After 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biotin serum (pmol/L)</td>
<td>195–300</td>
<td>98</td>
<td>124</td>
<td>260</td>
<td>204</td>
</tr>
<tr>
<td>Bisnorbiotin (pmol/L)</td>
<td>50–300</td>
<td>37</td>
<td>48</td>
<td>61</td>
<td>55</td>
</tr>
<tr>
<td>Total biotin metabolites (pmol/L)</td>
<td>300–500</td>
<td>156</td>
<td>225</td>
<td>364</td>
<td>325</td>
</tr>
</tbody>
</table>

digestion and unable to interfere with the intestinal absorption of biotin.

Biotin is widely present in nature, but the amount is low, compared with the other B-vitamins. Moreover, a large amount of biotin is not readily absorbable, because of its binding with protein (Table 1).

It is an essential nutrient because, during evolution, mammals have lost the ability to synthesize it. Biotin seems to regulate and ameliorate glucose homeostasis, because it favors an anti-hyperglycemic effect (with the above said enzymes) and hyperglycemic effect (with the regulation of the hepatic phosphoenolpyruvate carboxykinase, a gluconeogenic enzyme) [3].

According to the biotin roles as a regulator of intermediary metabolism and gene expression, its deficiency may cause decreased cellular proliferation, impaired immune and cerebral function and cutaneous manifestations. Some of the symptoms of biotin deficiency are thinning hair, often with loss of hair color, confusion, lethargy, progressing to coma, vomiting, seizures, dystonia, dysarthria, dysphagia, quadripareisis, ataxia, hypertension, chorea, paralysis of the seventh nerve, conjunctivitis, ketolactic acidosis and organic aciduria, seizures and mild hyperammonemia, breathing problems, developmental delay, skin rash, candidiasis, and perioral exudative skin rash.

The involvement of biotin in fat synthesis is often cited as a reason for dermatologic problems. Fat production is important for skin cells since they die quickly, and must be replaced very rapidly, and they are in contact with the outside environment and serve as a selective barrier to substances outside the body. When cellular fat components cannot be made properly, skin cells are among the first cells to develop problems.

The second most common set of clinical features of biotin deficiency involves nervous system problems. Nerve related symptoms have been linked to biotin deficiency because glucose and fat are used for energy within the nervous system, and biotin also functions as a supportive vitamin. If left untreated, neurologic clinical features can develop, including mild depression, which may progress to profound lassitude and, eventually, to somnolence, changes in mental status, generalized muscular pains (myalgias), hyperesthesias and paresthesias. A peripheral neuropathy, which is most common in patients who develop this condition from either long-standing diabetes or on-going hemodialysis, occurs in the nerves of the extremities, most commonly the feet and the calves [4]. Neurosensory hearing loss and eye problems, such as optic atrophy, have been described in many untreated children [4, 5].

Other symptoms are correlated with immunologic and metabolic abnormalities as a consequence of biotin deficiency. Biotin deficiency affects spermatogenesis, causing a delayed spermatogenesis, a decreased number of spermatozoa, reduced testicular and serum concentration of testosterone and a sloughing of seminiferous tubule epithelium. Biotin improves testosterone levels, probably because it participates in the synthesis of local testicular factors [6].

Extensive laboratory testing with chemical, biologic and instrumental examinations did not lead us to a positive diagnosis in this case, and that, despite the continuous proliferation of new diagnostic tests, an accurate history and physical remain the cornerstone of sound clinical practice.

Moreover, the occupational and social histories were important in the determination of the cause of biotin deficiency.

We excluded in the pharmacological history of the patient: parenteral nutrition without biotin supplementation in patients with short-gut syndrome; the use of anticonvulsant drugs, prolonged use of oral antibiotics, alcoholism (that reduces blood concentrations, hepatic content, urinary excretion, gastric disease, inflammatory bowel disease, severe protein-energy malnutrition [7–12].

In a patient with neurologic and dermatological signs, with a normal CT scan and NMR, additional testing is warranted, including examination of biotin status to confirm the diagnosis of biotin deficiency. Biotin deficiency is rare, so one must think of the possibility to confirm the diagnosis and initiate biotin supplementation.

Conflict of interest statement The authors declare that they have no conflict of interest related to the publication of this manuscript.

References