**Table S1. Characteristics of headache in the patient based on a retrospective questionnaire.**

| | |
|---|---|
| **Starting age** | 11 years, coinciding with menarche |
| **Family history for headaches** | Negative |
| **Initial location of pain** | Frontal region between the eyes |
| **Successive location of pain** | Frontal region |
| **Type of pain** | Pulsating and continuous |
| **Average pain level (1–10 scale)** | 7 |
| **Worst pain level (1–10 scale)** | 10 |
| **Average frequency** | Three to four headaches per week |
| **Frequency of the most severe bouts** | Four to five headaches per month |
| **Average duration** | Not determinable because the patient took analgesics within 1–2 hours from the onset of pain |
| **Time of occurrence during the day** | Variable |
| **Seasonality** | Not significant, even if headaches were more frequent after sun exposure |
| **Triggering factors** | Stress, meal consumption, menstrual cycle, pregnancy, insomnia, sun exposure and bright lights |
| **Impact on quality of life** | Important impact on daily activities without prompt analgesic treatment |
| **Pre-headache symptoms** | Cenesthesic symptoms, amaurosis fugax (one time) and sleep disorder |
| **Associated symptoms during the bout** | Increased sensitivity to light, nausea, vomiting, tachycardia, poor concentration, confusion and behavioral changes |
| **Improvement factors** | Darkness and analgesics |
| **Drugs for acute pain** | Acetylsalicylic acid; Ibuprofen |

**Table S2. Main results of biochemical tests performed in the patient during the last acute episode (52 years of age) after initiation of arginine therapy.**

| **Plasma Metabolite** | **Measured Value** (μmol/L) | **Normal Value** (mol/L) |
|---|---|---|
| Citrulline | 30 | 17–53 |
| Glutamine | 809 | 399–823 |
| Arginine | 197 | 38–135 |
| Ornithine | 266 | 25–159 |
| Alanine | 584 | 206–498 |
| **Urine metabolite** | **Measured Value** (mmol/mol creatinine) | **Normal Value** (mmol/mol creatinine) |
| Citrulline | 8 | 0–4 |
| Glutamine | 65 | 20–76 |
| Arginine | 764 | 0–5 |
| Ornithine | 314 | 0–5 |
| Alanine | 56 | 16–68 |
| Orotic acid | 0.74 | 0.2–1.1 |

Plasma citrulline and glutamine were normal; plasma arginine, ornithine and alanine were conversely increased. Urinary glutamine, alanine and orotic acid were normal; increased urinary excretion of citrulline, arginine and ornithine was also detected. These findings were inconclusive for UCD diagnosis but could be compatible with a UCD during treatment.