Introduction Periodic fever syndromes (PFSs) can present with a myriad of nonspecific signs and symptoms, with acute onset fever as the hallmark.

Case description We present the case of a 2-year-old boy who was admitted on 3 occasions with episodes of sudden onset isolated fever (40°C). From his history we noted 2 more hospital admittances in another medical center with similar presentations; also, the mother reported 4 more isolated fever episodes, the first at 4 months of age, during which the fever was apparently uninfluenced by antipyretics and disappeared after 3–5 days (no inflammatory markers were taken then as he was treated as an outpatient). A detailed history showed a clear periodicity of the episodes, occurring at 28–30 days intervals. Other symptoms were intermittently present during episodes: macular rash, unilateral cervical adenopathy (2 cm). Fever duration was 3 to 5 days, without a specific response to antipyretic or antibiotic treatment. A slight response to oral prednisone therapy was noted. At each admission, preliminary laboratory studies showed a marked inflammatory response (high CRP, procalcitonin, VSH, WBC). Broad spectrum antibiotic treatment was promptly started after blood and urine were sampled for cultures, as the presentations were interpreted at that time as high suspicion of occult sepsis/bacteremia. All sources of infection were ruled out each time by negative cultures. Blood smears and imaging studies did not raise any suspicion of malignancy. Tests for a primary immunologic defect were negative. PFSs were partially excluded as ANA titers, rheumatoid factor, IgD level was normal (HIDS), urinary mevalonic acid (MKD) was undetectable. Also, a genetic panel including 32 gene mutations/variants associated with PFSs including Familial Mediterranean Fever, CAPS, TRAPS, Blau syndrome, HIDS, ELANE related neutropenia and PAPA, did not detect mutations. All inflammatory markers returned to normal in between fever episodes. Our patient developed 3 more similar episodes, then the symptoms spontaneously stopped. The child is presently healthy, 6 months apart from the last episode.

Discussion PFSs are a diagnostic challenge. The key to a correct clinical approach is close monitoring of episodes and extensive workup. It seems that some causes remain undetected despite diagnostic efforts or, as in our case, have a self-limited evolution. Future research in this pathology is still necessary.