FINAL DIAGNOSIS:

Variant RARA translocation in a case with suspected APML but negative AML multiplex PCR .

DISCUSSION:

The majority of patients with acute promyelocytic leukemia (APL) manifest a specific chromosomal translocation t(15;17)(q22;q21), characterized by the fusion of RARA and PML genes. A subgroup of acute leukemia with morphology resembling acute promyelocytic leukemia (APL) shows variant translocations involving RARA and has a different morphology from that of classical APL. The variant APL with t(11;17)(q23;q12); ZBTB16-RARA subgroup has been reported to have leukemic cells with regular nuclei, many granules, absence of Auer rods, an increased number of Pelgeroid neutrophils, strong myeloperoxidase (MPO) activity. These cases constitute 1% of all APML cases. From a therapeutic point of view, t(11;17) APL is characterized by poor response to ATRA, resulting in an unfavourable prognosis. It was at first suggested that this resistance to treatment resulted from the ability of the ZBTB16 moiety to bind corepressors, but it has been proven that ZBTB16-RARA leukemia cells can fully differentiate on ATRA treatment. A better clinical response has been observed in the patients who received ATRA plus intensive chemotherapy.

CONCLUSION:

This case illustrate the importance of a comprehensive diagnostic work-up and importance of karyotyping in identifying abnormalities of clinical significance which may not be identified on PCR. The present study also emphasizes the importance of combining morphologic, immunophenotypic, cytogenetic, and molecular studies to distinguish variant APL cases from classical APL cases before initiating chemotherapy, regardless of whether the morphological study reveals findings consistent with those of classical APL.