PB1816 CHEMOTHERAPY FREE APPROACH IN A PEDIATRIC PATIENT WITH VERY LATE CUTANEOUS RELAPSE OF ACUTE PROMYELOCYTIC LEUKEMIA.

Valeria Crisci1, Emanuela Rossitti2, Giuseppina Aloj3, Pio Stellato3, Giuseppe Menna3, Rosanna Cuccurullo4

1 Pediatric, Università degli Studi di Salerno, Salerno, Italy; 2 Pediatric, Università degli Studi di Napoli Federico II, Naples, Italy; 3 Oncology, AORN Santobono- Pausilipon, Naples, Italy; 4 Oncology, AORN Santobono- Pausilipon, naples, Italy

Background:
Acute Promyelocytic Leukemia (APL) is a very rare leukemia in children. At diagnosis it is frequently fatal but at the same time highly curable through the combination of all-trans retinoic acid (ATRA) and anthracycline-based chemotherapy. Extramedullary involvement by APL can be observed in about 3-5% of cases, mainly during the relapses, and the most affected sites are the central nervous system, the skin, and the testes.

Aims:
To report on the use of arsenic trioxide (ATO) combined with ATRA in a pediatric patient with very late APL extramedullary relapse.

Methods:
A.M., a 14-year-old female, was admitted to our hospital with post-traumatic ecchymosis and metrorrhagia. Trilinear cytopenia and coagulopathy were present at diagnosis. Bone marrow aspirate showed an infiltrate of immature myeloid cells with features of promyelocytes. Molecular analysis by RT-PCR showed expression of the PML/RARa fusion protein. Standard Risk APL was diagnosed. The patient was treated according to protocol AIEOP ICC-APL 01 SR as front-line therapy. At the end of the induction the first complete haematological remission was achieved, while the first complete molecular remission was obtained at the end of the first consolidation cycle.

Three years and seven months after the onset of the disease, a skin lesion appeared on her back. A biopsy was performed and a promyelocytic infiltrate was found. The diagnosis was confirmed by the immunohistochemical analysis. Bone marrow aspirate, lumbar puncture and total body Computed Tomography did not show any further site of relapse. Thus, an Isolated Extramedullary Very Late Relapse (more than 36 months after the onset of the disease) of APL was diagnosed.

Although the best therapeutic option for APL relapses was still controversial at that time, the patient was treated with the most updated approach, receiving an induction cycle of 30 days with the association of ATRA at the dose of 25 mg/m2/die and ATO at the dose of 0.15 mg/Kg/die and a consolidation with 4 cycles of ATO (5 days per week, 4 weeks on and 4 weeks off) and 7 cycles of ATRA (7 days per week, 2 weeks on and 2 weeks off). The treatment was well-tolerated, except for sporadic occurrence of headache and an isolated episode of generalized seizures.

Results: The patient completed the treatment 8 months later and actually, 5 years after the relapse, is in complete haematological and molecular remission.

Summary/Conclusion:
Several large multicenter studies have shown that regimens combining upfront ATRA with chemotherapy lead to high remission rates in APL. However, relapses still occur in 15% to 25% of cases. Extramedullary involvement is extremely rare at relapse, especially in pediatrics. Salvage therapy should be chosen considering the previous front-
line therapy and is followed or not by auto or alloHSCT depending on the achievement of molecular remission.

The presented pediatric case did not receive the association ATO-ATRA in front-line because it was not available in that era. Therefore, she received the association ATO-ATRA in second line, obtaining the second complete remission with a chemo-free regimen.

This case shows that the association ATO-ATRA as single therapy in pediatric patients is safe and effective also for relapses and that the best second line therapeutic regimen should be chosen considering the treatment history of each patient.