es in secondary cases.2,8-10 h-M DS is considered a new entity, outside the FAB classification but related to refractory anemia.1,2,4 Evolution to MDS has been observed in the follow-up of non-transplanted patients with AA. Since prognosis and treatment are different in both entities, differential diagnosis is important. As detection of clonality is not possible in many cases,1,2,5 differentiation is based predominantly on morphologic parameters.

Half of our cases with h-M DS had an irregular distribution of hemopoiesis. Presence and morphology of megakaryocytes were more important criteria than features of erythroblasts and granulocytes. However, since no single new parameter enabled us to differentiate the two diagnostic groups clearly, a linear discriminant analysis was performed. Using an algorithm based on the combination of the four new parameters described, nearly 90% of the cases could be correctly classified. The jackknife procedure showed that the model was stable and we could create therefore an index which can be used easily in daily practice.

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Key words
Aplastic anemia, myelodysplasia, megakaryocytes, bone marrow histology, linear discriminant analysis

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References

Parotid and central nervous system relapse during complete hematological remission in acute promyelocytic leukemia

Sir,

Extramedullary leukemic infiltration is rarely observed in patients with acute promyelocytic leukemia (APL).1 To our knowledge only 32 cases of extramedullary APL have been reported.1-10 The extramedullary sites reported are skin, soft tissue, gingiva, breast, mandible, thymus, mediastinum, lymph node, spleen, liver, colon, optic nerve, external auditory canal and central nervous system (CNS). Some of these cases had extramedullary relapse with bone marrow in remission.1 Some authors hypothesize that all-trans retinoic acid (ATRA) treatment for APL may be associated with an increased incidence of extramedullary disease at the time of relapse,1,4-6 although a direct causal link has not been established, and this hypothesis lacks, at present, any statistical confirmation. The majority of the previously reported patients with extramedullary APL were treated only with standard cytotoxic chemotherapy.2

In June 1984, a 13-year-old girl presented with morphologically classic APL. A cytogenetic examination demonstrated 46XX, t(15;17) in all 20 cells analyzed. After a month the patient gained complete remission (CR) with daunorubicin and received consolidation and maintenance chemotherapy with alternating cycles of POMP, TRAP and COAP. Her disease remained in hematologic and cytogenetic remission until August 1996, when she presented with headache and a left parotid tumor. Excisional biopsy of the parotid revealed extramedullary APL.

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sphere consistent with leukemic infiltration of the CNS (Figure 1A). Cerebrospinal fluid cytology was negative. Peripheral blood and bone marrow studies including cytogenetic and molecular analysis, were normal at that time.

Treatment was initiated with ATRA, 45 mg/m²/day, in two divided oral doses. After five weeks of therapy the parotid tumor disappeared and post-treatment CAT of the brain showed disappearance of the CNS lesion on day 50 (Figure 1B). The patient received consolidation and maintenance chemotherapy.

After 22 months of second CR the patient developed APL hematologic relapse, her bone marrow karyotype was 46XX, t(15;17) and molecular analysis by RT-PCR revealed the presence of the PM L/RAR-α fusion gene without evidence of extramedullary APL. At the time of writing this report the patient is receiving induction therapy in order to reach a new hematologic remission.

This report confirms the efficiency of ATRA treatment for extramedullary APL, as previously observed.¹ ² ₅ ₈ ₁₀ To our knowledge this is the first report of extra-medullary relapse in the parotid in APL and the patient with the longest survival time in CR before extra-medullary relapse.¹ ₆ This extramedullary relapse occurred in a patient not previously treated with ATRA. Further information of extramedullary relapses in APL patients will undoubtedly contribute towards elucidating the real role played by ATRA therapy in this type of relapse.

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Key words
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Figure 1. Cranial CAT. A: pre-treatment; B: post-ATRA treatment.