The prognosis of NHL of the genital tract seems to be favorable, even when the tumor is extensive.[8] According to one study the 5-year survival is 70%, and the most important predictive factor is the stage according to the Ann Arbor classification.[9]

Diagnosis of genital tract lymphoma is frequently delayed by the lack of specific symptoms, the commonest disturbances being bleeding, discomfort and vaginal discharge. The tumor is usually infiltrative and colposcopy biopsy may give false negative results, as in this case. This rare disease must be kept in mind in the differential diagnosis of the genital tract pathologies, because it can present at any age and may mimic other diseases of the vagina clinically and pathologically.[10] In standard management of lymphoma only stage I disease and, depending on grading and histologic subtype, stage II are treated exclusively with radiotherapy, whereas chemotherapy alone or in combination with radiotherapy is used in all other stages. Primary involvement of the vagina can be successfully treated by pelvic radiation, but cytotoxic chemotherapy should be considered in young woman to preserve fertility.

In conclusion we state that the polychemotherapy is a useful and effective treatment of vaginal NHL which concomitantly protects fertility.

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Key words

Non-hodgkin lymphoma, vagina, chemotherapy, and fertility.

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Homozygous Constant Spring: the first case described in the West

In this work we present the clinical and laboratory data and the molecular identification of homozygosly for Constant Spring in an Argentinian man with parents of Sicilian origin (Palermo). The presence of this in the homozygote form in the West and the difficulty of detecting it in heterozygotes by classical methods suggest that probably more cases eixist.

Sir,

α-thalassemias are a group of diseases caused by reduced synthesis of alpha globin chains. They can be classified into α^+ or α° thalassemia depending on whether the synthesis is totally or only partially absent. Hemoglobin Constant Spring (Hb Cs Sp) is the principal cause of non-deletion α-thalassemia in South-East Asia and Southern China.[1,2] This is caused by a mutation in the terminal codon of the α_2 globin gene (TAA-CAA)[3] which extends the transcription producing an unstable α_2 mRNA that encodes a protein of 172 residues instead of the 141 residues in normal globin. Thalassemic expression and the very low levels of Hb Cs Sp produced are caused by instability of α_2 mRNA and its intracytoplasmatic degradation.[4]

We present the clinical and laboratory data and the molecular identification of an Argentinian man of Sicilian origen.

He had had hemolytic anemia since childhood with splenomegaly and had received blood transfusions on several occasions.

Blood study revealed Hb 9.2 g/dL; RBC 4×10^{12}/L; PCV 32%; MCV 80 fL; MCH 23 pg; reticulocytes 8%. The quantification of Hb Cs Sp+HbA_2 was 8.6% and the HbF of 2.5%. Red blood morphology showed anisocytosis, moderate hypochromia, abundant target cells and basophilic stippling.

The possibility of an α-thalassemic deletion was ruled out by Southern blot and α_2 gene amplification followed by digestion with Hph and Nco I restriction enzymes screen out the existence of a specific mutations corresponding to the non-deletion α-thalassemias α^{Hph} and α^{Nco}. The fragments obtained after digestion with Mse I restriction enzyme correspond to a homozygote for some mutation in the region of the

Table 1. α_2 gene amplification (product 1943bp) followed by digestion with *Mse* I, *Nco* I and *Hph* enzymes: the fragments obtained.

		Haplotype		
RE	$\alpha\alpha$	$\alpha^*\alpha$	$\alpha^{NCO}\alpha$	$\alpha^{Hph}\alpha$
Mse I	1379, 401,163 bp	1379, 563 bp	-	-
Nco I	1094,849 bp	-	1943 bp	-
Hph	1078,322,236,163, 97,32,15 bp	-	-	1395,236,163, 97,32, 15 bp

*– without anormal fragments; *mutation in the region of the terminal codon of the α_2 gene (Constant spring, Icaria, Seal Rock and Koya Dora). RE: restriction enzyme.*

terminal codon of theα_2 gene (Table 1, Figure 1 A).

The specific allele amplification for Hb Constant Spring (TAA-CAA) and Icaria (TAA-AAA) was only achieved with the specific primer for Hb Constant Spring (Figure 1 B).

Hb Cs Sp has been previously described in heterozygous form associated to a deletional α^+-thalassaemia in Greek and Sicilian families,[5] nevertheless, our case is the first case of homozygosity for Hb Cs Sp identified in the West.

It is noteworthy that heterozygous forms ($\alpha^{CS}\alpha/\alpha\alpha$) are difficult to detect by classical techniques[3,6] because production of Hb Cs Sp is very low (0-1%) and basic haematologic data are normal.

Homozygosity for Hb Cs Sp was manifested by hemolysis, moderate anemia, jaundice and splenomegaly.[6] This is because accumulation of αCS has deleterious effects on the red blood cells due to changes induced by binding of oxidized αCS with the membrane which augments membrane rigidity and its mechanical stability and alters cell hydration producing severe hemolysis.[7]

Our patient clinical and laboratory data correspond to those found in other homozygotes from South-East Asia. We suspect that other cases probably exist but, because of the difficulty of identifying the heterozygous form, remain undetected.

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Key words

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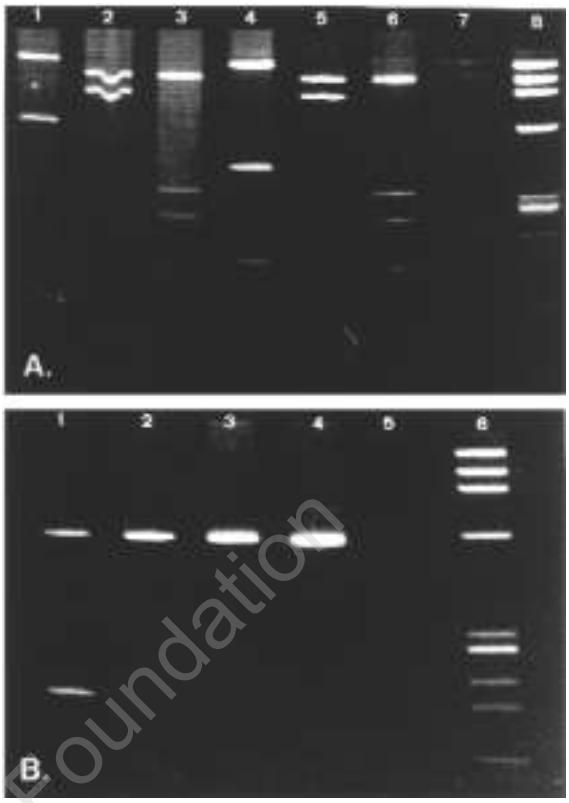

Figure 1.
A. Acrylamide gel electrophoresis of the Mse I, Nco I, Hph digest of the amplified DNA from homozygous Hb Cs Sp and control. Lane 1 trough 3 DNA from patients homozygous Hb Cs Sp digest with Mse I, Nco and Hph respectively. Lane 4 trough 6 DNA from control digest with Mse I, Nco and Hph respectively. Lane 7 contamination control. Lane 8 DNA size marker $\Phi \times$ 174 RF.
B. Strategy for direct detection of the Hb Cs Sp and Hb Icaria allele in the α2 gene. A fragment from α2 gene was amplificated by PCR using the primers 5'- GTAAACACCTC-CATTGTTGG-3' and a mutagenic primers, for Hb CsSp allele 5'-GCTGACCTCCAAATACCGTC-3' and for the Hb Icaria allele 5'-GCTGACCTCCAAATACCGTA-3'. Another pair of primers were used like internal control of amplification C_D: 5'-GGCCTAAAACCACAGAGAGT-3' and C_R: 5'- CCAGAAGC-GAGTGTGTGGAA-3'. Lane 1 and 3 are the amplified products with Hb Cs Sp specific primers. Lane 2 and 4 are the amplified products with Hb Icaria specific primers. Lane 1 and 3 DNA patient with homozygosis Hb Cs Sp. Lane 2 and 4 DNA negative control. Lane 5 contamination control. Lane 6 DNA size marker $\Phi \times$ 174 RF.

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Liver nodular regenerative hyperplasia after bone marrow transplant

We report an unusual liver disease which may occur after bone marrow transplantation, i.e. the collapse of hepatic lobuli followed by regenerative islets: the resulting clinical picture may mimic GvHD or a viral disease, but histology is diagnostic, showing nodular regeneration in the absence of inflammation or fibrosis.

Sir,

Liver abnormalities are frequently detected after bone marrow transplantation (BMT). Early after the transplant they may be due to drug toxicity, less frequently to venocclusive disease (VOD), viral or septic infection. Late liver impairment is often related to chronic graft-versus-host disease (GvHD), and less frequently to viral reactivation or drug toxicity. Persisting disorders are also to be expected in patients who survive a VOD.[1] A rarer post-transplant liver disorder is *nodular regenerative hyperplasia* (NRH), which is characterized by the formation of intrahepatic nodules of regenerating hepatocytes, with moderate or no fibrosis. This disorder has been associated with a number of clinical conditions of autoimmune (rheumatoid arthritis; Sjögren's, CREST or Felty's syndrome), hematologic (myelo-and lymphoproliferative disorders), or endocrine (diabetes mellitus) origin,[2] or even after prolonged administration of immunosuppressive[3] or contracceptive drugs. We report the case of a patient who had NRH nine months after an allogeneic BMT.

A 35-year old male with chronic myeloid leukemia in chronic phase received a bone marrow transplant from his HLA-identical brother in March 1998. The conditioning regimen was BuCy2; he was infused with 1.6×10^8/kg. GvHD prophylaxis was a short course of cyclosporin A and methotrexate (MTX). On day +2, after the first dose of MTX, the patient developed weight gain, painful hepatomegaly, decreased diuresis and increased bilirubin, transaminases and PAI-1. With the suspicion of an impending VOD, we discontinued MTX and all signs and symptoms disappeared. On day +33, a grade IV acute cutaneous GvHD occurred, successfully treated with high dose prednisone. At +5 months the patient presented with increased ALT, AST, γ-GT, ALP and bilirubin, in the absence of markers of viral infection. The patient was thought to have hepatic GvHD, so she underwent liver biopsy, which showed liver injury probably due to drug toxicity. All drugs were discontinued, and all liver function parameters improved; however, three months later a new wave of hepatic cytolysis and cholestasis occurred (Figure 1). A repeat liver biopsy showed hepatocyte nodular regeneration with compression of the surrounding tissue, in the absence of inflammatory cells even in portal areas and virtually no fibrosis. This picture is typical of NRH (Figure 2). No treatment was planned; liver enzymes are checked every month and continue to fluctuate. Seven months after the diagnosis of NRH, no sign of portal hypertension has appeared.

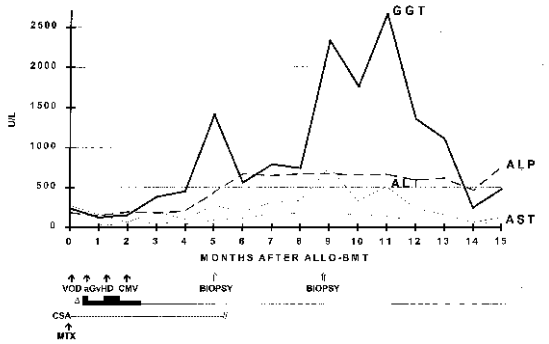

Figure 1. Post-transplant time course of liver enzymes.

The pathogenesis of NRH is not well understood. Probably it results from sinusoidal lesions causing local hypoperfusion with regenerative hyperplasia in the normally perfused surrounding areas.[4] Clinically, NRH may be confused with liver cirrhosis.[5] Fifty per cent of patients with NRH develop portal hypertension.[4] Hepatic failure, rupture of the liver, malignant transformation and gastric antral vascular ectasia syndrome are described complications of NRH.[6,7]

It is possible that post-transplant NRH is more frequent than reported, since several cases could have been clinically misdiagnosed as VOD, GvHD or drug toxicity.[8] Since no clinical or laboratory findings are specific to NRH, an informative liver biopsy is the only key to a correct diagnosis.[9] In addition, since the liver may be sequentially involved by a number of different events in the post-transplant period, repeat liver biopsies may be necessary to identify all the damaging mechanisms.

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Key words

NRH, BMT, GvHD, Liver Biopsy, LMC

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