Skin changes in POEMS syndrome

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The so-called POEMS syndrome is a multisystemic disorder characterized by the association of polyneuropathy, organomegaly, endocrinopathy and skin changes. These disorders seem to be secondary to a plasma cell dyscrasia leading to production of a monoclonal component. Several other signs can occur, e.g. anasarca, pyrexia, finger clubbing, sweating and hematologic disorders.

The syndrome has been described mainly in Asians, although some Caucasian cases have been reported.[1,2] We report the images of skin changes which appeared in a 39-year-old Caucasian male; all the other above mentioned signs were also present. The diagnosis of POEMS syndrome was established in April 1987. The patient developed a progressive peripheral polyneuropathy with demyelination, hepatosplenomegaly, sclerotic bone lesions, scleroderma and IgGλ monoclonal gammopathy. Bone marrow examination showed about 9% plasma cells of apparently normal morphology. Two years later the patient had a myocardial infarction with transient thrombocytosis together with papilledema. A consistent improvement was obtained with plasmapheresis, chemotherapy (melphalan) and high dose prednisone. After a further three years severe polyneuropathy reappeared, with symmetrical motor and sensory deficiencies in the limbs, peripheral edema, pleural effusion, hypogonadism and hypothyroidism. Treatment with melphalan, cyclophosphamide and plasmapheresis together with prednisone was not very effective. Since September 1997 the patient has had rapid, progressive appearance of multiple skin angiomas (50-60, several tuberous), together with dermal fibrosis with sclerodactylia, pleural and myocardial effusions, pyrexia and capillary leak syndrome. A slight improvement was obtained using high dose dexamethasone and this has been maintained up to now with intermittent dexamethasone treatment.

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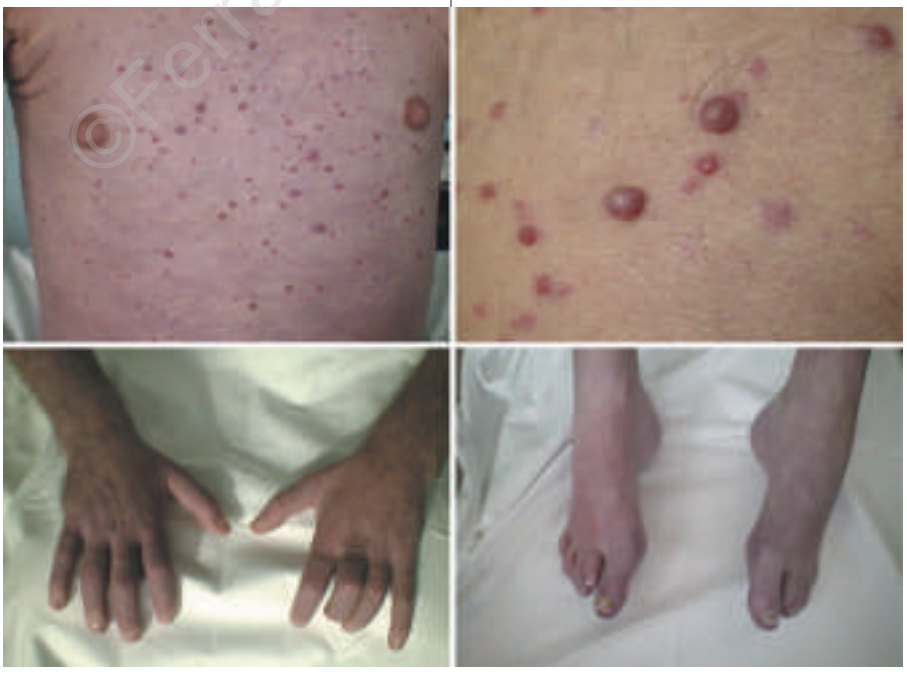

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Existence of a hypercoagulability state prior to prosthetic hip or knee surgery

Sir,

we compared the values of D-D, TAT, and F1+2 before hip or knee arthroplasty in 79 elderly patients with those of 33 age-matched control subjects. The levels of D-D and TAT were significantly higher in patients than in controls. This hypercoagulability state may be attributed to the ostheoarticular disease and supports the appropriateness of starting antithrombotic prophylaxis prior to surgery.

Patients subjected to substitutive surgery of the hip or knee are a group acknowledged to be at increased risk for venous thromboembolic disease (VTED). It has been suggested that the condition of orthopedic patient is one of the most important risk factors; the papers by Francis *et al*.[1] concerning hip arthroplasty, and those of others investigators on knee prosthesis[2,3] support this affirmation. The hypothesis is that a presurgical state of hypercoagulability could be detected by appropriate tests.

The aim of this work was to evaluate the levels of several hypercoagulative markers in patients with hip or knee pathology before surgery.

We studied 79 consecutive elderly patients admitted for total hip or knee replacement. The control group consisted of 33 similarly aged healthy subjects. In both groups the levels of the following markers were studied (before surgery in the experimental group): D-D, with the ELISA VIDAS D-DIMER® kit (BioMerieux, Marcy-L'Etoile, France), with normal reference levels between 68-494 ng/mL. TAT and F 1+2 were assayed by ELISA with the kit Enzignost® micro (Behringwerke AG, Marburg, Germany); normal reference levels being 1.0-4.1 mg/L and 0.4-1.1 nmol/L for TAT and F1+2, respectively. The characteristics of all groups are summarized in the Table 1. Figure 1 shows the box-plots for the three markers in the study groups. The original values of D-D have been transformed into their "Ln"(equal to "n log") for graphics and statistical analysis because of their asymmetrical distribution and the fact that the range of values was extremely wide. The Anova test was performed on this variable for comparison between groups. The levels of D-D were significantly higher in patients with hip pathology than in controls (F = 4.58; p=0.012), but not in patients with knee pathology. The Kruskall-Wallis test was used for comparison of the variables TAT and F 1+2. Significant differences were found between the three groups for TAT levels (χ^2 = 9.12; p= 0.001), with higher values in the patients with hip or knee disease than in the controls; F1+2 did not differ between the groups (χ^2 = 4.1; p=0.12). We want to emphasize that TAT and D-D plasma levels in the patient groups were not only higher than the average levels specified by the manufacturers of the kits but also higher than those of the healthy subjects of similar age. However, our control group also showed levels of D-D and F1+2 superior to the average for the kit, possibly due to their advanced age.[4-6] The selection of elderly control subjects was, of course, intentional in order to have a population equivalent to the patient groups.

The predictive value for VTED of some hypercoagulative markers has been reported in abdominal[7,8] and in hip surgery,[9,10] though it was not an objective of this work, because systematic screening for VTED with confirmatory tests was not performed.

The potential induction of an hypercoagulability state by the same ostheoarticular process present in the orthopedic patient, counsels the appropriateness of starting antithrombotic prophylaxis previously to arthroplasty.

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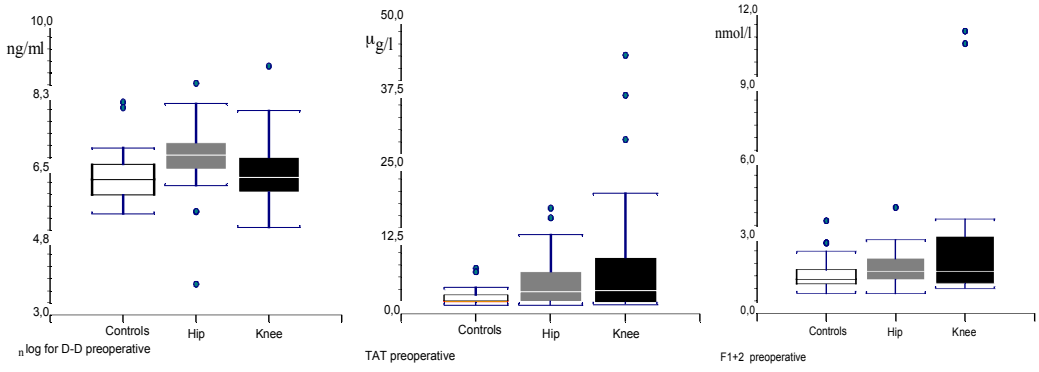

Figure 1. The central line of the box is the median (50% percentile); the lower level represents the 25% percentile; the higher limit represents the 75% percentile; the line over the box represents the value of the 75% percentile plus 1.5 times itself; the line below the box represents the 25% percentile minus 1.5 times itself; the dots represent outlying data.

Table 1. Baseline demographic characteristics and mean values for the three hypercoagulative markers in the patients and in the control subjects.

Variable	*Hip*	*Knee*	*Controls*
Number of cases	53	26	33
Age (years)			
Mean	64	67	68
Percentiles 25-75%	60-73	64-70	62-73
Sex			
Male	27	3	17
Female	26	23	16
Indication for surgery *(more than one diagnosis could be present in the same patient)			
Osteoarthrosis	39	23	–
Necrosis	10	1	–
Rheumatoid arthritis	7	2	–
Miscellaneous	2	2	–
Markers			
Mean			
D-D (ng/mL)	1,135.5	847.4	727.5
TAT (µg/L)	5.3	9.0	2.8
F1+2 (nmol/L)	1.7	2.6	1.5
Percentiles 25-75%			
D-D (ng/mL)	665.14-1,339.43	403.42-992.27	365.03-812.4
TAT (µg/L)	2.1-7.6	2.05-9.8	2-2.9
F1+2 (nmol/L)	1.4-2.1	1.3-3.0	1.2-1.7

Keys words

Hypercoagulability, hip and knee arthroplasty, venous thromboembolic disease

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Cryptic insertion (15;17) in a case of acute promyelocytic leukemia detected by fluorescence *in situ* hybridization

Sir,

We report the case of a patient with acute promyelocytic leukemia (APL) with no detectable cytogenetic abnormalities. Fluorescence *in situ* hybridization (FISH) studies demonstrated an insertion of the RARα gene into one copy of chromosome 15. RT-PCR studies showed a PML/RARα transcript. The patient achieved complete remission with chemotherapy and ATRA, but relapsed during maintenance therapy with ATRA.

Acute promyelocytic leukemia (APL) is characteristically associated with the reciprocal chromosomal translocation t(15;17)(q22;q21) which is identified in up to 90% of cases by conventional cytogenetics. However, a few cases with submicroscopic rearrangements of RARα gene have been described.[1]

A 27-year-old man was admitted to our hospital because of a one-week history of weakness and fever. Blood cell count showed: Hb 79 g/L; WBC 45×10^9/L with 79% hypergranular blast cells and platelets 39×10^9/L. The bone marrow findings were consistent with classical APL (AML-M3) according to the FAB criteria. The immunophenotype showed: $CD13^+$, $CD33^+$, $HLA\text{-}DR^-$ and $CD34^-$. He was treated according to the European APL/93 protocol (ATRA in combination with cytosine arabinoside and daunorubicin) and achieved a complete remission on day 30 of treatment. The patient relapsed, 20 months after diagnosis, during maintenance therapy with ATRA. A second remission was obtained with Ara-C, mitoxantrone and etoposide. Afterwards, he received an allogeneic peripheral blood stem cell transplantation (PBSCT) from his HLA-identical sister. The patient developed a veno-occlusive disease and acute graft-versus-host dis-