Primary Plasma Cell Leukemia

Sir,

Plasma cell leukemia (PCL) is a rare neoplastic disease characterised by plasma cell proliferation in the bone marrow with invasion of peripheral blood and internal organs. The diagnosis of PCL is made when the absolute number of plasma cells in the peripheral blood is more than $2 \times 10^9$ litre or more than 20% of the circulating white blood cells. PCL is classified as primary and secondary. Primary PCL is the de novo appearance of PCL without prior occurrence of multiple myeloma and when PCL occurs as a terminal event in multiple myeloma, it is known as secondary PCL.

The reported incidence of PCL ranges from 1.6% to 5% in different series, however primary PCL is very rare and the incidence is not reported. Only three cases in Indian literature and 67 cases in Western literature are reported between 1965 and 1986. We describe a case of primary PCL for its rarity.

A 55-year male came with complaints of abdominal pain, fullness in the epigastric region, breathlessness on exertion and fatigue for 15 days. Investigations revealed that there was no H/O multiple myeloma in the past. His laboratory investigations were: Hemoglobin 8.6 gms%, total leukocyte count 45000 cells/cu. mm., differential count: polymorphs - 16%, lymphocytes - 06 %, plasma cells - 78 % NRBCS - 2/100 WBCs, platelet count 60000/cumm and ESR 110 mm. at the end of one hour, peripheral smear showed normocytic normochromic RBCs, leukocytosis with plasma cells in varying stages of maturation with many immature forms (Fig. 1). Platelets were reduced.

Bone marrow examination revealed hypercellularity with 62% plasma cells in varying stages of maturation (Fig. 2). Binucleated and multinucleated forms were seen. Serum calcium was 10.5 mgs%, serum phosphorus 4.1 mgs%, blood urea nitrogen 38 mgs%. Urine showed albumin +, BJ protein ++, 24 hour urinary protein - 3.6 gms/24 hours, serum protein electrophoresis showed “M band”. USG abdomen showed moderate hepatosplenomegaly. X-ray chest and skull showed no osteolytic lesion.

The diagnosis was given as primary plasma cell leukemia.

Plasma cell dyscrasias are a common group of disorders having the proliferation of a single clone of immunoglobin secreting cells as a common feature. The incidence of various plasma cell dyscrasias is as follows: 1) Monoclonal gammopathy of undetermined significance: - MGUS - 60 to 70%. 2) Multiple myeloma 15%. 3) Amyloidosis 9%. 4) B cell lymphoproliferative disorders: Non-Hodgkin’s lymphoma 5%, WM 2%, CLL 2%. 5) Solitary plasmacytoma 1%. 6) Plasma cell leukemia - Rare.

Primary PCL is characterized by a short history of symptoms of anemia, bleeding episodes, generalized weakness, weight loss, hepatosplenomegaly and absence of osteolytic lesions. Our case had all these features except bleeding manifestations.

Plasma cells noted in the peripheral blood frequently demonstrate marked nuclear immaturity with prominent nucleoli. Our case also showed many immature plasma cells in the peripheral blood.

A unique feature of PCL, which should be noted, is the relatively high proportion of cases associated with IgE paraprotein; however our case had IgG paraprotein.

Primary PCL is treated by chemotherapy, irradiation, autologous bone marrow transplantation and interferon, but prognosis is poor; death occurring within one year.

SR Desai*, NN Angarkar**, AG Kulkarni+
*Professor and Head; **Associate Professor; Department of Pathology, KIMS Karad; +Principal, Pravara Medical College, Loni, Dist. Ahmednagar.

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Tuberous Sclerosis in a Family with Varied and Rare Manifestations

Sir,

Tuberous sclerosis previously known as epiloia is an autosomal dominant disorder characterized by hamartomas mainly in the brain (tubers), skin (adenoma sebaceum, ash-leaf macules, shagreen patch and periongual fibromas), kidneys (angiomyolipomas, multiple cysts), heart (rhabdomyoma), lungs (interstitial fibrosis) and liver (hamartomas).1 Seizures and mental retardation are essential and presenting features; while renal involvement can occasionally occur. Familial occurrence is rare. We are reporting a family (a father and daughter) who had tuberous sclerosis with varied initial manifestations.

A 37 year male (father) presented to us with history of breathlessness with features of uraemia of 5 months duration and severe right sided abdominal pain in flanks past 7 days with no history of haematuria and seizures.

Examination revealed hypertension (BP 170/120 mm Hg), skin lesions (Fig. 1) in the form of adenoma sebaceum. The abdominal examination revealed bilateral palpable kidneys. Fundus revealed grade II hypertensive retinopathy. Investigations revealed moderate renal insufficiency (blood urea 90 mg%, serum creatinine 3.2 mg%, proteinuria of 1 g/day and GFR 32 ml/min). Haemoglobin was 10 g%, serum calcium 8.5 mg% and phosphorus 6.0 mg%. ECG showed left ventricular hypertrophy. X-ray chest revealed cardiomegaly.

CT scan head (Fig. 2) showed calcified lesion in left paraventricular area. USG of abdomen revealed bilateral enlarged kidneys with multiple cysts proved to be polycystic kidney disease on intravenous pyelography with poor excretory function especially of the right side.

His daughter was 12 years old who had tonic-clonic seizures at the age of 9 months with delayed milestones due to mental retardation. On examination, she also had adenoma sebaceum, Shagreen patch and there was renal involvement of kidneys on ultrasonography in the form of multiple cysts. Kidney functions were normal. Intravenous pyelography revealed polycystic kidneys.

The clinical features of both father and the daughter are summarised in Table 1.

Renal cysts or angiomyolipomas have been a rare manifestations of tuberous sclerosis and when present usually remain asymptomatic in early childhood.2 It is apparent that father might have renal cysts in childhood which remained asymptomatic for many years till he developed features of renal failure. This fact is supported by the presence of multiple cysts with normal renal functions in the daughter.

Our patient (father) did not have mental insufficiency and seizures till now in spite of advanced renal involvement with failure; while the daughter had both seizures and mental insufficiency in the childhood. This could be due to spontaneous mutation in a patient with tuberous sclerosis with cystic kidneys.3

This family report stresses the vertical transmission with gene mutation in the family members. The varied clinical manifestation in the father and the daughter in the same family with cystic kidneys in both of them are of rare occurrence, hence, reported.

Table 1: Shows clinical features of both father and daughter

<table>
<thead>
<tr>
<th>Age and Sex</th>
<th>Seizures</th>
<th>Mental retardation</th>
<th>Skin lesions</th>
<th>Renal cysts</th>
<th>Hypertension</th>
<th>Renal function</th>
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<tbody>
<tr>
<td>Father</td>
<td>37 M</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Deranged</td>
</tr>
<tr>
<td>Daughter</td>
<td>12 F</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Fig. 1: Plate shows; A - Adenoma sebaceum, B - Shagreen patch over back (indicated by arrows)
Fig. 2: CT scan shows calcified lesion in paraventricular area (arrows)

SN Chugh*, S Atri**, P Mittal***, Navdeep***
*Associate Professor and Incharge Endocrine and Metabolism,
**Senior Resident, ***Resident, Department of Medicine, Pt. B.D. Sharma PGIMS, Rohtak.
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Successful Steroid Therapy in Multiple Sclerosis Presented as Acute Psychosis

Sir,

Although psychiatric disorders are common in cases with multiple sclerosis (MS), psychosis is a rare associated feature or complication in this condition. Use of high dose of steroid in such demyelinating disease is likely to have more risk of developing psychosis. However, this case report argues against the relation between steroids and psychosis particularly in demyelinating cerebral disorder.

Although depression is more common in patients with multiple sclerosis (MS) occult MS presenting as psychosis is very rare. We wish to report a case of multiple sclerosis presented as ‘acute and transient psychotic disorder’ (ATPD), which did not improve with antipsychotic medication and finally responded very well to steroid. To our knowledge, this is the first case of such kind reported in the English literature. Previously, similar case was illustrated only in Spanish literature.2

Ms. A, 20 years old girl presented with history of irrelevant talk, being suspicious, multimodality hallucinations and neglecting personal care of one month duration.

Three months prior to the onset of current illness, she developed numbness in all limbs and had difficulty in walking. MRI brain at that time revealed multiple hyper-intensities in right peri-ventricular area, corpus callosum and white matter areas. She was diagnosed as multiple sclerosis by a neurologist on the basis of MRI and electrophysiological findings. She was treated successfully with prednisolone 20mg for one month at different hospital. There was no history of drug abuse, confusion and persistent mood symptoms.

Her mental state examination revealed fearful behaviour, delusions of persecution and reference, visual hallucinations such as seeing fire and olfactory hallucinations such as smell of burning, auditory hallucinations of commanding nature, illusions and also had active negativism. Her cognitive functions were grossly intact and no abnormal neurological signs were elucidated. Provisional diagnosis of ATPD, polymorphic type was made as per ICD-10 criteria.

She was treated with chlorpromazine 600mg and trifluperazine 15mg for 4 weeks without improvement. Even parental haloperidol 30mg per day for five days did not alleviate psychotic symptoms. Her repeat MRI showed the same findings suggestive of MS. Hence all antipsychotic drugs were replaced by prednisolone 10 mg/day, which was further increased to 40mg/day over a period of two weeks, as advised by the neurologist. For sleep disturbance, thioridazine 50mg/day was given for three weeks. She showed dramatic improvement with prednisolone and later on same drug was tapered over a period of 4 weeks. Subsequently, she was put on carbamazepine 400mg per day as she was complaining of numbness in all extremities. Patient was followed up for 3 years without recurrence of psychotic symptoms.

This case was presented to us as only ATPD without any associated neurological features. This showed that florid symptoms of psychosis can obscure neurological symptoms in MS as seen in previous studies or psychiatric symptoms may precede the neurological symptoms in some cases of MS.

Peculiarity of this case is that the psychosis was resistant to psycho-pharmacotherapy and responded well to steroid. On the basis of this finding, our opinion is that steroid can improve psychosis if it is related to demyelination as observed in another case report.2 Atypical antipsychotic drug such as clozapine has been successfully tried to treat psychosis associated with multiple sclerosis.4

In our case the exact lesion of the CNS that is responsible for psychosis is difficult to establish due to multiple sites of lesions. Feinstein et al found that only trend of a higher total lesion score, particularly around the periventricular area in a psychotic group of MS patients when compared to non-psychotic group of MS patients. In this case also frank psychotic features were associated with periventricular hyper-intensities. It is difficult to generalize our finding based on only single case report. More systematic study is needed on large number of patients to find out whether steroid can be effective in cases of psychosis associated with demyelinating disorder.
DN Mendhekar*, R Mehta**, V Puri†
*Assistant Professor, †Post Graduate Student, Dept. of Psychiatry; ‡Professor and Head, Dept. of Neurology, G.B. Pant Hospital, New Delhi.
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Multiple Recurrences of Tuberculosis in an HIV Infected Individual

Sir,

We report a severely immunosuppressed HIV-infected patient with multiple recurrences of tuberculosis proved to be due to re-infection by DNA fingerprinting.

A 33 years male presented with complaints of productive cough, breathlessness and high-grade fever of two months duration. He was found to be HIV-1 positive by ELISA and confirmed by Western Blot. He was anemic and CD4 count was 24 cells/mm³ (4%) and the CD4:CD8 ratio was 0.06. A diagnosis of smear positive pulmonary tuberculosis was made and was treated with WHO Category I regimen by directly observed therapy (DOT). Sputum culture and drug susceptibility testing for mycobacteria revealed Mycobacterium tuberculosis sensitive to all first line anti-tuberculous drugs. The patient responded well to anti-TB treatment, sputum smears and cultures became negative by the 2nd month of treatment and he was declared cured at the end of six months.

The patient developed a recurrence after two months and was treated with WHO Category II DOT. At this time his CD4 counts were still very low (4 cells per cumm, 1%). Sputum culture grew M. tuberculosis sensitive to all first line drugs. The patient responded well to therapy but continued to stay in the hospital for social reasons. Three months after completing Category II treatment, the patient developed a recurrence and this time the drug susceptibility results showed M. tuberculosis resistant to isoniazid. The patient was treated with a regimen containing streptomycin, rifampicin, ethambutol and pyrazinamide daily. The patient became sputum smear and culture positive again after eight months and this time M. tuberculosis resistant to isoniazid and rifampicin was isolated from the sputum. As soon as the drug susceptibility results became available, the regimen was changed to include kanamycin, ofloxacin, ethambutol, pyrazinamide and ethionamide, with good response.

Fig. 1 shows the restriction fragment length polymorphism (RFLP) pattern using three probes IS6110, direct repeat (DR) and polymorphic GC rich sequence (PGRS) of M. tuberculosis isolated from the patient initially and during two of the relapses (20, 28 months), using the standard protocol. Recurrent tuberculosis might be due to either relapse or exogenous re-infection.1,2 In this case, recurrent TB was due to re-infection. Though data from India is limited, previous work from this center has shown that re-activation contributes to about two-thirds of relapses in HIV negative subjects.3 There have been no reports from India on TB recurrences in HIV positive individuals. One interesting finding of our report is that infection caused during the 3rd and 4th episode was by a new strain, which was identified only by DR RFLP and not by the other two probes. Although RFLP using IS6110 is the internationally accepted standard method for DNA fingerprint studies on M. tuberculosis strains, it has several limitations in developing countries. Multiple probes increase the sensitivity and discriminatory power of DNA fingerprinting.

Nosocomial transmission of TB has been reported to occur and is particularly frequent among immuno-suppressed individuals. A policy of separating smear positive from smear negative patients would be ideal in hospitals admitting TB patients and wherever possible HIV infected persons should be segregated from infectious TB patients. The contribution of re-infection to the epidemiology and pathogenesis of tuberculosis has important implications for tuberculosis control in India and other countries with a high burden of HIV and tuberculosis and deserves further study.
Massive Increase of Insulin Resistance in a Patient with Chronic Hepatitis C After Treatment with Interferon

Sir,

A 63 kg, 52 yr woman with diabetes mellitus for 15 yrs was stable on a daily insulin dose of 44 units. From 1997 she was known to have chronic Hepatitis C. In September 2001, she was started on alfa interferon 3 million units sc twice weekly. During the course of treatment, she developed ascites and went into Child’s Stage 2 by January 2002. Interferon treatment was discontinued from 10th January 2002. The patient’s diabetes was out of control from Nov 1999, and she had to be admitted for stabilization in mid Jan 2002.

During admission insulin was administered via syringe pump with frequent glucose monitoring by finger prick. Within 24 hrs it became obvious that she would need very large doses of insulin. Ultimately her blood glucose was stabilized between 7 and 10 mmol/l (126-180 mg/dl) on 700 iu of regular insulin administered by syringe pump. During all this time she remained in Child Stage 2. There was no evidence of infection or malignancy. There was a past history of pulmonary tuberculosis which had been adequately treated, and presently mRNA for Mycobacterium tuberculosis was negative in the ascitic fluid.

On the 4th day, the insulin requirements started to drop and the urine became high colored. Within 12 hours, her liver parameters worsened and she went into Child Stage 3. Insulin was stopped and standard treatment for hepatic precoma was instituted. The patient responded to treatment and could be discharged home after 26 days in hospital. Her daily insulin dose on discharge was 26 units and within a month it increased to 30 units. The blood glucose is currently maintained between 10 and 15 mmol/l (180 to 270 mg/dl) and she continues to have mild ascites.

The patient continued to remain well and ultimately lapsed into hepatic coma in November 2003 and died.

No factor other than alpha interferon could be associated with this dramatic and transient rise of insulin requirement. Insulin resistance is known to be increased by interferon alpha and transient diabetes has been recorded. Destabilization of diabetes of this magnitude has not been reported before.

S Chatterjee
Park Clinic, 4 Gorky Terrace, Kolkata-700 017, India
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REFERENCE

Announcement


Venue : Hotel Jehan Numa Palace, Shamla Hills, Bhopal (MP).

Under Auspices of ICP, ICC, ISCPT, API MP, API CH, WC Railways and IMA Bhopal.

For any information please contact : Dr. PC Manoria, Organizing Chairman, CDE Summit - 04, E-5/103, Arera Colony, Bhopal 462016.

Tel. : 0755-2422299; Mobile : 9827074602; E-mail : pmanoria@rediffmail.com