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The 23-Valent Polysaccharide Pneumococcal Vaccination is Not Useful in BMT Patients at Risk of Pneumococcal Bacteremic Sepsis

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Introduction: Long term survivors after BMT are at risk of serious infections with encapsulated bacteria, in particular, *streptococcus pneumoniae*. BMT patients in our center received a 23-valent polysaccharide pneumococcal vaccine six months after transplantation but the efficacy of vaccination remained undefined and fulminant pneumococcal bacteremic sepsis has occurred in vaccinated patients. We investigated the risk factors for pneumococcal infections post BMT and assessed the efficacy of pneumococcal vaccine by measuring the antibody levels before and after vaccination. **Patients and Methods:** Medical records from 482 survivors after BMT in Queen Mary Hospital from January 1995 to December 1999 were reviewed. Nine patients had documented pneumococcal sepsis defined as the presence of *streptococcus pneumoniae* in blood cultures with clinical sepsis. Patients were analysed according to the development of chronic graft-versus-host disease (cGVHD), the use of total body irradiation (TBI) in the conditioning regimen and the source of BMT. The humoral response to pneumococcal vaccination was measured by immunoassays on paired serum before and two week after vaccination. Radio-isotope liver and spleen scans were also performed to assess the splenic function of BMT patients who had developed pneumococcal bacteremic sepsis. **Results:** The median age of the patients was 32 years (range 8 m - 67 yr). 147 patients received TBI during conditioning. 363 patients received allogeneic BMT in whom 103 had developed cGVHD. 119 patients received autologous transplant. TBI and a combination of allogeneic BMT and cGVHD significantly increased the risk of pneumococcal bacteremic sepsis ($p< 0.05$). There was no significant increase in antibody titre in BMT patients after pneumococcal vaccination in contrast to the 3 to 4-folds increase in immunocompetent controls. Nine patients have developed pneumococcal bacteremic sepsis. In four patients, infections resulted in septic shock requiring intensive care one of whom developed overwhelming sepsis leading to multi-organ failure and death within 24 hours of hospital admission. Five patients have received pneumococcal vaccination before. 99^{m}Tc Colloid liver and spleen scan were performed in six patients and revealed the absence of splenic uptake in one patient and significantly reduced uptake in three others. Two patients had normal splenic uptake. **Conclusion:** TBI and cGVHD were significant risk factors for pneumococcal infection after BMT and the polysaccharide pneumococcal vaccine was of no protective value. Further studies are needed to evaluate the optimal prophylactic strategy in high risk patients.

S-HM-12

Methylation of *p15* and *p16* Gene Promoters in Gastric Lymphoma

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Background: The stomach is the commonest site of extranodal B cell non-Hodgkin's lymphoma (NHL). The two most usual lesions are diffuse large cell (DLC) lymphoma and Mucosa associated lymphoid tissue lymphoma (MALToma). Hypermethylation of the promoters of the tumor suppressor genes *p15* and *p16* leading to gene silencing has been found in high grade NHL.

Patients and Method: DNA from 29 patients with gastric lymphoma and 30 patients with nodal lymphomas were studied. These patients were matched for clinicopathologic parameters. Genomic DNA was extracted from the sample and was then bisulfite-modified. The modified DNA was amplified by the methylation specific polymerase chain reaction (MS-PCR) for the detection of methylation in *p15* and *p16* promoters.

Results: MALToma has higher frequencies of *p15*, *p16* and concomitant *p15/16* methylation than gastric DLC lymphoma (72% vs 39%, 81% vs 61% and 64% vs 22%). However, gastric DLC lymphoma has comparable frequencies of *p15* and *p16* methylation as nodal DLC lymphoma.

Conclusion: In gastric lymphoma, *p15/p16* promoter methylation may be important in the pathogenesis of MALToma. Furthermore, as demethylation of *p15* and *p16* promoters is not known to happen, the lower frequency of *p15/p16* methylation in gastric DLC lymphoma as compared with MALToma argues against a transformation to the former from the latter. The reason why there is a higher frequency of DLC lymphoma than MALToma in the stomach in Chinese patients remains to be defined.