Conclusion: There is a high incidence of nodal metastases in patients with malignant pleural mesothelioma and the pattern of nodal metastases may be different from that of lung cancer and multicenter study is needed to study this subject accurately.

**P1-106 Mesothelioma and Other Thoracic Malignancy Posters, Mon, Sept 3**

**Evaluation of SV-40 as a biological prognostic factor in Egyptian patients with malignant pleural mesothelioma**

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**Background:** Malignant Mesothelioma is a highly aggressive primary neoplasm of the pleural, peritoneal, and pericardial surfaces. It is a challenging disease in all aspects, from presentation and diagnosis to staging and treatment. In the past 50 years, the incidence of malignant pleural mesothelioma (MPM) has been increasing especially in developing countries, along with industrial development. The association between simian virus (SV40) and malignant pleural mesothelioma (MPM) suggests an etiological role for SV40. However, exact pathogenic mechanisms and possible prognostic value are not clear. Transformation of human cells by SV40 is induced by the large tumor antigen (Tag) and the small tumor antigen (tag). The main mechanism(s) by which the Tag induces cell transformation and tumorigenesis is via the inactivation of key cellular proteins, such as p53 and pRB family proteins.

**Methods:** Fresh tumor tissues were obtained from 40 MPM Egyptian patients presenting at NCI, Cairo. Of them, 22 were from extra-pleural pneumonectomy specimens and 18 from thoracoscopic biopsies. All cases were diagnosed as MPM and graded using World Health Organization (WHO) criteria on hematoxylin and eosin-stained sections combined with immunohistochemistry and clinical features. All cases diagnosed as MPM were positive for mesothelioma markers (calretinin, mesothelioma antigen, keratin 5/6) and negative for epithelial membrane antigen and/or cytokeratin and/or CEA. Sarcomatoid cases were diagnosed by being positive for mesothelioma antigen and negative for vimentin. The samples were also investigated for the presence of SV40 DNA, altered Rb expression and p53 gene status using immunohistochemistry and molecular techniques. Patients were staged according to the International Mesothelioma Interest Group (IMIG) staging system. The relation between SV40, asbestos exposure, Rb, p53 and their contribution to clinicopathologic characteristics and overall survival (OS) were assessed.

**Results:** The age ranged from 20 to 69 years (mean= 45± SD), 21 were males and 19 were females. SV40 DNA was detected in 20/40 cases and asbestos exposure in 31 cases; 18 of them were SV40 positive. Altered p53 and Rb expression were detected in 57.5% and 52.5% respectively with no p53 mutation. There was a statistically significant correlation between the presence of SV40 viral sequences and the pathologic type of the tumor since 13 out of the 20 SV40 positive cases (65%) were of the sarcomatoid/mixed variants compared to 7 (35%) of the epithelioid variant (p = 0.03). Similarly, there was a statistically significant correlation between the presence of SV40 viral sequences and a positive history of asbestos exposure (p = 0.03). Univariate analysis showed a significant correlation between OS and stage (p=0.03), performance status (p=0.04), p53 overexpression (p=0.05), asbestos exposure (p =0.002) and SV40 (p=0.001). Multivariate analysis showed that when SV40 and asbestos exposure were considered together, only combined positivity of both is an independent prognostic factor affecting the OS (p = 0.001).

**Conclusion:** SV40 and asbestos exposure are common in Egyptian MPM denoting a possible etiological role and a synergistic effect for both agents. Our results prove that combined positivity for SV40 and asbestos exposure is an independent prognostic factor in MPM having a detrimental effect on OS.

**P1-107 Mesothelioma and Other Thoracic Malignancy Posters, Mon, Sept 3**

**Evaluation of Simian Virus-40 as a biological prognostic factor in Egyptian patients with malignant pleural mesothelioma**

Bahnassy, Abeer A.1 Gaafar, Rabab M.2 Zekri, Abdel-Rahman N.3 Mohamed, Waleed S.3 Hassan, Nelly A.4 Abdel-Rahman, Mohamed5 Abou-El-Kasssem, Fatma2

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**Background:** Malignant Mesothelioma is a highly aggressive primary neoplasm of the pleural, peritoneal, and pericardial surfaces. It is a challenging disease in all aspects, from presentation and diagnosis to staging and treatment. In the past 50 years, the incidence of malignant pleural mesothelioma (MPM) has been increasing especially in developing countries, along with industrial development. The association between simian virus (SV40) and malignant pleural mesothelioma (MPM) suggests an etiological role for SV40. However, exact pathogenic mechanisms and possible prognostic value are not clear. Transformation of human cells by SV40 is induced by the large tumor antigen (Tag) and the small tumor antigen (tag). The main mechanism(s) by which the Tag induces cell transformation and tumorigenesis is via the inactivation of key cellular proteins, such as p53 and pRB family proteins.

**Methods:** Fresh tumor tissues were obtained from 40 MPM Egyptian patients presenting at NCI, Cairo. Of them, 22 were from extra-pleural pneumonectomy specimens and 18 from thoracoscopic biopsies. All cases were diagnosed as MPM and graded using World Health Organization (WHO) criteria on hematoxylin and eosin-stained sections combined with immunohistochemistry and clinical features. All cases diagnosed as MPM were positive for mesothelioma markers (calretinin, mesothelioma antigen, keratin 5/6) and negative for epithelial membrane antigen and/or cytokeratin and/or CEA. Sarcomatoid cases were diagnosed by being positive for mesothelioma antigen and negative for vimentin. The samples were also investigated for the presence of SV40 DNA, altered Rb expression and p53 gene status using immunohistochemistry and molecular techniques. Patients were staged according to the International Mesothelioma Interest Group (IMIG) staging system. The relation between SV40, asbestos exposure, Rb, p53 and their contribution to clinicopathologic characteristics and overall survival (OS) were assessed.

**Results:** The age ranged from 20 to 69 years (mean= 45± SD), 21 were males and 19 were females. SV40 DNA was detected in 20/40 cases and asbestos exposure in 31 cases; 18 of them were SV40 positive. Altered p53 and Rb expression were detected in 57.5% and 52.5% respectively with no p53 mutation. There was a statistically significant
correlation between the presence of SV40 viral sequences and the pathological type of the tumor since 13 out of the 20 SV40 positive cases (65%) were of the sarcomatoid/mixed variants compared to 7 (35%) of the epithelioid variant (p = 0.03). Similarly, there was a statistically significant correlation between the presence of SV40 viral sequences and a positive history of asbestos exposure (p = 0.03). Univariate analysis showed a significant correlation between OS and stage (p = 0.03), performance status (p=0.04), p53 overexpression (p=0.05), asbestos exposure (p=0.002) and SV40 (p=0.001). Multivariate analysis showed that when SV40 and asbestos exposure were considered together, only combined positivity of both is an independent prognostic factor affecting the OS (p = 0.001).

Conclusion: SV40 and asbestos exposure are common in Egyptian MPM denoting a possible etiological role and a synergistic effect for both agents. Our results prove that combined positivity for SV40 and asbestos exposure is an independent prognostic factor in MPM having a detrimental effect on OS.

P1-108 Mesothelioma and Other Thoracic Malignancy Posters, Mon, Sept 3

Clinical features of endotracheal / endobronchial metastases: analysis of 55 cases

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Objective: To discuss the clinical presentation, diagnosis and treatment of endotracheal/endobronchial metastases (EEM).

Methods: Retrospective and follow-up analyses were conducted of 55 cases of bronchoscopically confirmed EEM. Clinical staging, location in the tracheobronchial tree, the number of lesions, treatment and prognosis were analyzed.

Results: The most common neoplasms associated with EEM were esophageal carcinoma (50.9%) and gastric cancer (9.1%). Most EEM patients presented with cough, hemoptysis, dyspnea, chest pain and fever. Abnormal changes on chest X-ray were found in 83.6% cases, and CT imageological changes were found in all patients. There were 29/66 lesions in the trachea, and 37/66 in the bronchus, including 18 in the right bronchus and 19 in the left bronchus. Type I EEM accounted for 22/66 cases; Type II, 20/66 cases; Type III, 10/66 cases, and Type IV, 14/66 cases. The median survival time was 8.1 months. There was significant difference in survival time between Type IV EEM and the other three types.

Conclusion: EEM may occur in the trachea or in the bronchus. Flexible bronchoscopy is a valuable tool for the diagnosis of EEM. Although there are cases of long survival, the prognosis of EEM is generally poor.

P1-109 Mesothelioma and Other Thoracic Malignancy Posters, Mon, Sept 3

Genetic metabolic polymorphisms and risk of pleural mesothelioma

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Background: Malignant pleural mesothelioma (MPM) is a rare and aggressive cancer. Asbestos fibers exert their well-recognized causative effect on MPM through the direct or indirect generation of reactive oxygen and nitrogen species. Many genes that encode for xenobiotic and oxidative metabolism enzymes are polymorphic, resulting in possible individual differences in cancer risk. Two previous studies related the risk of MPM with few genetic polymorphisms of xenobiotic and oxidative metabolism enzymes, as assessed by PCR techniques, generating the hypothesis that genetic variation may have a role in individual susceptibility to MPM. An association study performed in a case-control setting including 90 MPM patients and 395 referent subjects is described. Thirtyfive single nucleotide polymorphisms (SNP) in 10 genes of phase I and 27 SNPs in 8 genes of phase II of the xenobiotic metabolism were explored in relation to the risk of MPM.

Methods: The polymorphisms were analyzed all at once for a given sample by a micro-array technique based on the arrayed-primer extension (APEX) principle.

Results: After adjusting for multiple comparisons according to the Wacholder method, a general lack of statistically significant association was evident, with the exceptions of CYP1B1 and NAT1. The homozygotes carrying the variant R48G within CYP1B1 were found at about four-fold increased risk of MPM respect to homozygotes wild type (OR=4.22, 95% CI 1.68-10.61, p=0.002). In addition, the ORs calculated for the diplotypes showed that there were haplotypes associated with the risk of MPM. The slow and intermediate acetylator phenotypes for NAT1 posed an increased risk of MPM respect to the fast acetylator genotype (OR=4.46, 95%CI 1.07-18.63 and OR=2.35, 95% CI 1.03-5.4, respectively).

Conclusions: The present study reinforces the hypothesis that the acetylator-phenotype plays a role in relation to the etiology of MPM and suggests CYP1B1 as a novel risk factor for MPM.

P1-110 Mesothelioma and Other Thoracic Malignancy Posters, Mon, Sept 3

The dosimetric effects of changes in thoracic cavity fluid levels during adjuvant hemithoracic intensity modulated radiotherapy following extrapleural pneumonectomy for mesotheliomas

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Background: Malignant pleural mesotheliomas are rare tumours involving the pleural lining of the lung, often associated with asbestosis. We offer aggressive tri-modality treatment in carefully selected patients, consisting of neoadjuvant chemotherapy (cisplatin and pemetrexed) followed by extrapleural pneumonectomy followed by adjuvant hemithoracic intensity modulated radiotherapy (IMRT). Usually the thoracic cavity (TC) becomes completely fluid filled after surgery and is stable throughout treatment. However, in some patients, the TC is partially filled at the beginning and the fluid levels may change during radiation. Clearly, increasing the density of the TC contents will tend to attenuate the dose delivered (and vice versa). However, the magnitude of these effects are not well understood. The aim of this study is to investigate the clinical significance of these dosimetric effects.

Methods: The patient was planned using the Inverse Planning module of the Pinnacle treatment planning system (version 7.6c). Appropri-