**480. Diagnosis and biology of malignant pleural effusions**

**P4616**
The bedside autofluorescence pleuroscopy for the undiagnosed lung cancer with pleural effusion in a intensive care unit

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**Introduction:** Autofluorescence bronchoscopy was developed to enhance the detection of lung cancer in the airway. However, its role in evaluation of pleural space has not been published.

**Aim:** To assess the undiagnosed lung cancer with pleural effusion in an intensive care unit (ICU).

**Methods:** A flexible bronchoscope (SAFE 3000, Pentax, Tokyo) to entry to assess the pleural space. The evaluation of pleural space was started by Twin Mode and then completed by MIX. Then the specimens send for histological examination and the clinical data retrospectively studied. The whole procedures were done in the ICU bedsides.

**Results:** 22 patients were recruited. There were 6 patients with cytology negative and normal finding in WLP or AFP but 2 of them were found to have lung cancer. Among the 16 patients with atypia or suspicious cells had abnormal finding in the WLP or AFP, 15 patients finally had lung cancer.

**Conclusion:** The AFP is useful for detecting the undiagnosed lung cancer with pleural effusion. This is a daily practice performed not only in endoscopic room but in the ICU bedsides.

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**P4617**
Triple chemotherapy (paclitaxel/gemcitabine/cisplatin) is more active in advanced squamous cell subtype (SCC) non-small cell lung cancer (NSCLC) than doublet treatment (vinorelbine/cisplatin): A randomized phase III trial in 443 NSCLC patients

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**Background:** A triplet regimen of Paclitaxel/Gemcitabine/Cisplatin was compared to a standard doublet regimen to examine for superiority.

**Patients and methods:** Histologically verified inoperable NSCLC patients (pts) were randomized to A (paclitaxel 180 mg/m² and cisplatin 100 mg/m² day 1 with gemcitabine 1000 mg/m² day 1 and 8 every 3 weeks) or to regimen B (cisplatin 100 mg/m² day 1 and weekly i.v. vinorelbine every 4 weeks).

**Results:** 443 pts were randomized (A: 221; B: 222). Median age was 62 years (range 38-75 years) overall, 58% were males, 11% had PS 2, 62% stage IV disease, 46% adenocarcinoma, and 28% SCC, equally distributed between A and B. Both regimens had median 4 treatment courses. Toxicities were largely similar in A and B. Response rates were 43% and 39% in A and B, medians of progression free survival (PFS) were 6.7 and 5.8 mths (p=0.453), and median overall survivals (OS) were 11.4 and 10.8 mths (p=0.415), respectively. PFS and OS were significantly higher in A than in B in SCC subtype (median PFS 7.0 mths vs. 4.1 mths, p=0.001; median OS 13.5 mths vs. 9.7 mths, p=0.020). Response rates were equal (52% vs. 38%, p=0.129).

**Conclusions:** Triplet paclitaxel/gemcitabine/cisplatin was not superior to doublet vinorelbine/cisplatin in advanced NSCLC. However, the triplet regimen had significantly higher activity compared to the doublet in SCC. This superiority in SCC may likely be due to gemcitabine being more active than vinorelbine in this subtype though the relative contribution of paclitaxel remains to be determined.

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**P4618**
Evaluation of pleural fluid human epididymis 4 (HE4) as a marker of malignant pleural effusions

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**Pleural effusions** are a commonly encountered problem in clinical practice, and pleural fluid analysis is usually the first step towards identifying the underlying etiology. Numerous studies have been published analyzing the potential utility of measuring biomarkers in pleural fluid as possible indicators of a malignant effusion, however there are no studies that have examined the presence of HE4 in pleural effusions. The aim of this study was to assess pleural effusion and serum concentrations of HE4 in patients with different types of pleural effusions and to evaluate the diagnostic performance of HE4 in detecting malignant pleural effusions.

**Patients and methods:** A prospective study was carried out of 88 consecutive patients presenting with pleural effusions. The patients were divided into three groups: 22 patients with transudative effusions, 32 patients with non-malignant exudative effusions and 34 patients with malignant pleural effusions. Blood and pleural fluid HE4 levels were measured using a chemiluminescent immunoassay.

**Results:** Both serum HE4 levels and pleural effusion HE4 levels were significantly higher in patients with malignant effusions than in patients with transudative or non-malignant exudative effusions. A pleural fluid HE4 cut-off value of 1675 pmol/L was found to predict malignant pleural effusions with a diagnostic sensitivity of 85.3% and specificity of 90.7%.

**Conclusion:** The current study reports a novel finding of increased serum and pleural fluid HE4 levels in patients with malignant effusions compared to non-malignant effusions. This finding has the potential to strengthen the diagnostic performance of tumor markers in detecting malignant pleural effusions.
P4619

Serum thioredoxin-1 as a diagnostic marker for malignant peritoneal mesothelioma
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Background: Diffuse malignant peritoneal mesothelioma (DMPM) is an aggressive malignant tumor of mesothelial origin that shows a limited response to cytoreductive surgery along with intra-peritoneal chemotherapy. Therefore, diagnosing DMPM early is very important. Reactive oxygen species (ROS) play an important role in asbestos toxicity, which is associated with the pathogenesis of DMPM growing. Thioredoxin-1 (TRX) is a small redox-active protein that demonstrates anti-oxidative activity associated with tumor growth. Here, we investigated the serum levels of TRX in patients with DMPM and compared them with those of a population that had been exposed to asbesstop but had not have DMPM.

Study: The serum concentrations of TRX were measured in 15 DMPM patients and 34 individuals with benign asbestos-related diseases.

Result: We demonstrated that the patients with DMPM had significantly higher serum levels of TRX than the population who had been exposed to asbestos but had not have DMPM.

Conclusion: Our data suggest that serum TRX concentration is a useful serum marker for DMPM.

P4620

Diagnostic value of vascular endothelial growth factor, glycosaminoglycan, cathepsin S, cathepsin H in the discrimination of transudate exudate and benign malignant patients with pleural effusion
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Pleural effusion is one of the most common problems and it was reported that 4% of the patients applying internal clinics suffer from pleural effusion. Cathepsin S, cathepsin H, glycosaminoglycan and vascular endothelial growth factor (VEGF) recently parameters are started to be investigated. In this study, 90 patients, who are diagnosed as pleural effusion, were searched proteine, glycos, pH, albumine, lactate dehydrogenase (LDH), coesterol, triglyceride, C-reactive proteine (CRP), amilase and also diagnostic value of cathepsin S, cathepsin H, glycosaminoglycan and VEGF parameters were investigated for the discrimination of transudate exudate and benign malignant patients with pleural effusions. PS/S cathepsin S, PS cathepsin H, PS/S cathepsin H, PS VEGF and PS/S VEGF parameters were found statistically significant (p=0.033, p=0.001, p=0.016, p=0.014, p=0.015). S cathepsinS, PS cathepsin H, PS/S cathepsin H, PS VEGF, PS/S VEGF, PS GAG parameters were detected statistically significant between transudate and exudate groups (p=0.037, p=0.008, p=0.009, p=0.001, p=0.001, p=0.016). There is a significant difference between malign and infectious groups for PS/S cathepsin S, PS cathepsin H parameters(p=0.028, p=0.020). As a result of our findings, VEGF, cathepsin S and cathepsin H could have a role in forming exsudate fluids especially in malign pleurisy and we concluded that they may be useful in the discrimination of malign benign fluids. It was considered that VEGF, cathepsin S, cathepsin H and GAG could be helpful in the discrimination of transudate exudate.

P4621

F-18 FDG PET scan 20 years after talc pleurodesis: Report of 3 cases
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FDG PET scan is used with increasing frequency to investigate pleural abnormalities and to determine the possibility of neoplastic invasion. Talc pleurodesis has been reported to cause hypermetabolic pleural thickenings and masses, up to 5 years after the procedure. We report 3 cases of patients who required talc pleurodesis for pneumothoraces in 1989 and 1990 with satisfying results, and who were investigated in 2010-2011 for pleural abnormalities, with positive TEP results, which were deemed secondary to the pleurodesis. Talc pleurodesis functions by creating inflammation, therefore promoting pleural adhesions. The metabolism surrounding this inflammatory reaction could decrease with time, as in other inflammatory processes. However, the fact that talc itself is not metabolized by the body would explain the positive FDG PET scan, possibly as a foreign body reaction.

We discuss radiological differences that can be used to differentiate between hypermetabolic talcosma and neoplastic disease.

Conclusion: Talc pleurodesis can induce an inflammatory reaction, even 20 years after being performed. In patients with pleural abnormalities, it is important to question such procedures and mention them to colleagues interpreting metabolic imaging.

P4622

Relevance of FDG-PET-CT scan for the evaluation of local pleural invasion assessed by thorascopy in malignant pleural mesothelioma
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Introduction: FDG-PET-CT scan(PET) is now widely recognized as an important staging modality in many cancers and PET standard uptake values(SUV) is reported as a prognostic indicator in several malignancies. However only a few previous studies have investigated the utility of PET in malignant pleural mesothelioma(MPM). We hypothesized that pleural assessed by PET might be in accordance to pleural characteristics evaluated by thorascopy.

Methods: 29 patients with a diagnosis of MPM obtained by thorascopy were previously evaluated byPET, and considered valuable for this analysis. Among them, 10.34%, 20.69%, 44.83%, 24.14% were assessed as I,II, III, IV stage respectively. There were 10.34% of patients in stage I, 20.69% in stage II, 44.83% in stage III, and 24.14% in stage IV. The histologic analysis showed 86.21% epitheloid, 3.45% sarcomatous and 10.34% biphasic types.

Results: At thorascopy there were 16 (55.17%) patients with visceral pleural involvement, 21 (72.41%) with diaphragmatic involvement and 2 (9.09%) with mediastinal involvement. All of them had an invasion of the costal parietal pleura. There was a significant difference (<0.05) of the medium SUV between the patients with a visceral pleural involvement and the patients without this feature. Moreover statistically significant differences of the medium SUV was shown between patients with or without pleural nodules.

Conclusions: These findings suggest that pleural evaluation by PET should in accordance to the characteristics obtained by thorascopy. There is a significant difference between the site of pleural involvement and/or the typology of tumoral lesions and the SUV of PET.
Cytology and DNA ploidy techniques in the diagnosis of malignant pleural effusion
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Introduction: Pleural fluid (PF) cytology is the first approach to diagnose malignant pleural effusion (MPE). Its sensitivity ranges from 40 to 80% and depends on the quality of slide preparation, histological tumor type and the cytopologist’s skill to differentiate tumor cells from benign reactive mesothelium. Ancillary methods are often required to improve the cytological diagnosis.

Objectives: To evaluate the sensitivity and specificity of conventional cytology, and the contribution of fluorescence in situ hybridization (FISH) and DNA ploidy in MPE diagnosis.

Materials and methods: PF samples from 85 patients were analyzed by cytology and classified as: malignant (presence of malignant cells; n=45; 52.9%); suspicious (presence of atypical cells; n=16; 18.8%) or benign (no malignant or atypical cells; n=24; 28.3%). FISH was performed in the 85 PF samples by the alpha, centromeric probes for chromosomes 11 (red) and 17 (green) and classified as normal or aneuploid according to the cut-off previously established. In 43 samples we also performed DNA ploidy by flow cytometry (FC). Patient’s records were consulted for definitive diagnosis.

Results:

<table>
<thead>
<tr>
<th>Method</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytology</td>
<td>93.2</td>
<td>80.7</td>
<td>89.4</td>
</tr>
<tr>
<td>FISH</td>
<td>94.8</td>
<td>96.1</td>
<td>94.2</td>
</tr>
<tr>
<td>DNA ploidy</td>
<td>59.5</td>
<td>33.3</td>
<td>55.8</td>
</tr>
</tbody>
</table>

Conclusion: FISH improved the cytological diagnosis of MPE. In five cases of suspicious and in three cases of negative cytology, the presence of aneuploidy cells reclassified the cases as MPE. In these cases, all patients were confirmed with cancer. CF DNA ploidy showed weak diagnostic performance.

We recommend associate FISH to cytology mainly for patients with previous diagnosis of cancer who develop pleural effusion with suspicious cytology.

P4625

Withdrawn

P4626

Ultrasound guided forceps biopsy of the pleura
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Background: Ultrasound guided forceps biopsy of the pleura is a technique that can cover the diagnostic yield gap between the needle biopsy of the pleura and thoracoscopy or thoracotomy. This technique enables the operator to take biopsy from multiple pleural sites.

Study objectives: (1) To describe the ultrasound guided forceps biopsy of the pleura as a technique that is not in common use in our practice to obtain pleural biopsy. (2) To evaluate the diagnostic yield of this technique in undiagnosed exudative pleural effusion.

Design: Prospective interventional study.

Setting: Ultrasound Unit- Chest Department- Assiut University Hospital - Egypt.

Patients and methods: All recruited patients (96) had exudative pleural effusion with first pleural tapping undiagnostic. Patients with bleeding tendency or blood coagulation defects were excluded. The procedure was performed under local anesthesia (Xylocaine 2%) and aseptic condition. The patients were premedicated by analgesic (Ketorolac thromethamine 20mg). Three to five biopsy fragments were obtained from each case and sent in 10% formaldehyde to the pathology laboratory. The diagnostic yield was compared with that of thoracoscopy.

Results: Compared to thoracoscopy the sensitivity in diagnosis of malignant and tuberculous lesions was 85% and 88% respectively. The technique was absolutely specific in diagnosis of malignant and tuberculous lesions.

Conclusions: Ultrasound – guided forceps biopsy of the pleura is a simple, efficient, and safe procedure. It can be carried out easily and safely even in sick and obese patients. On the other hand, the procedure appears similar to the thoracoscopy in obtaining adequate pleural tissue specimens. Yet, it is simpler and less traumatic.

P4627

How much of a role does immunohistochemistry have in reaching a final diagnosis of pleural malignancy in routine clinical practice?
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Introduction: Pleural fluid immunohistochemistry is not recommended in the routine pathological work up of a suspected malignant pleural effusion due to its low sensitivity. However, research has demonstrated its usefulness in diagnosing the primary site of a malignancy, particularly in adenocarcinomas. We wished to ascertain the frequency of its use and the contribution immunohistochemistry made to identifying the source of metastatic pleural deposits.

Methods: We retrospectively examined all pleural specimens sent for analysis over a 12 month period in patients with confirmed pleural malignancy. We noted the proportion of specimens stained for tumour markers and evaluated the contribution immunohistochemistry made to localising the primary source of the malignancy. These were grouped into three different categories: (i) undiagnostic, (ii) confirmatory and (iii) diagnostic.

Results: A total of 101 pleural specimens were sent for cytological and histological examination. Analysis revealed: 37 adenocarcinomas, 4 squamous cell carcinomas, 1 small cell cancer. 19 malignant mesotheliomas, 1 lymphoma and 1 schwannoma. 10 specimens were reported as malignant cells and 28 samples had no malignant cells present. 42 specimens had additional immunohistochemistry performed. In 2 specimens
immunohistochemistry was undiagnostic. It was a confirmatory test in 38% (n=16) and diagnostic in 47.6% (n=20).

Conclusion: We found that immunohistochemistry was underutilised, particularly when cytological analysis revealed malignant cells or adenocarcinoma. In the specimens where these tumour markers were used it was mostly diagnostic in localising the primary for adenocarcinomas.

P4628 The effect of a pleural diseases clinic on pleural effusion admission rates
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Background: Patients with pleural effusion are frequently admitted to hospital on the medical intake. Some of these admissions may be predicted and acute admission avoided.

Aim: A weekly specialist pleural diseases clinic was established in May 2011. We assessed whether provision of dedicated clinic time for patients who may require pleural intervention would reduce hospital admission rates of patients with pleural effusion.

Method: A retrospective review of electronic records for patients attending the clinic between 01/06/11-30/11/11. Hospital records were analysed for pleural effusion admission events (ICD10 codes J90/J91) in this period and between 01/06/10-30/11/10.

Results:

Table 1. Characteristics of patients attending the pleural diseases clinic

<table>
<thead>
<tr>
<th>Year</th>
<th>Mean age (years)</th>
<th>Malignant pleural effusion</th>
<th>Parapneumonic effusion</th>
<th>Paraneoplastic effusion</th>
<th>Other Non-Pulmonary Malignancy</th>
<th>Lung Adenocarcinoma</th>
<th>Other Lung Malignancy</th>
<th>Lung Adenocarcinoma</th>
<th>Pleural infection</th>
<th>Mesothelioma</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>68 (28–92)</td>
<td>47 (52.8)</td>
<td>16 (18)</td>
<td>17 (18)</td>
<td>14 (100)</td>
<td>14 (100%)</td>
<td>11 (83%)</td>
<td>12 (75%)</td>
<td>16 (18)</td>
<td>1 (54%)</td>
</tr>
<tr>
<td>2010</td>
<td>64 (25–82)</td>
<td>47 (52.8)</td>
<td>16 (18)</td>
<td>17 (18)</td>
<td>14 (100)</td>
<td>14 (100%)</td>
<td>11 (83%)</td>
<td>12 (75%)</td>
<td>16 (18)</td>
<td>1 (54%)</td>
</tr>
</tbody>
</table>

MPE, malignant pleural effusion; PPE, parapneumonic effusion; IPC, indwelling pleural catheter.

Conclusion: Development of a pleural clinic is associated with a reduced length of stay for patients admitted with pleural effusion. This could have significant cost-saving implications. However, the number of admissions increased by 219% over the study period. The cause of this rise is not clear.

P4629 Incidence of lung entrapment in malignant pleural effusion
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Introduction: Lung entrapment is commonly seen in patients with empyema and complicated parapneumonic effusions. However, the incidence of lung entrapment is not well reported in malignant effusions. We intend to report the incident in our patient who underwent pleuroscopy in 2011.

Method: A prospective observational study was performed on patients who underwent pleuroscopy in 2011 in Changi General Hospital (CGH). The findings on pleuroscopy were noted for all patients, in particular, the presence of lung entrapment. Biopsies of the parietal pleura were performed during pleuroscopy. Patients with biopsies positive for malignant pleural effusion were included in our analysis.

Results: In 2011, twenty four pleuroscopies performed in CGH. Fifteen (62.5%) were proven to have malignant pleural effusion on biopsy. Of these fifteen patients, 10 (66.7%) had lung carcinoma, 4 (26.7%) had breast carcinoma and the remaining patient (6.7%) had carcinoma of the cervix. Fourteen patients (93.3%) with malignant effusion were noted to have lung entrapment on pleuroscopy of various. Computed tomography scan (CT scan) of the lungs showed patency of the airway. However, bronchoscopy was not performed for these patients.

Conclusion: The incidence of lung entrapment is high in our patients with malignant pleural effusion. This will have an impact on the long term management of such patients. Our finding would suggest that talc pleurodesis may not be the best treatment options. The use of an indwelling pleural catheter may be a better option for our patients with malignant pleural effusion.
had significantly higher serum CRP levels at 24 h and 72 h than at baseline (p < 0.001). Mean serum CRP levels at baseline, 24th h and 72nd h were 4.5±3.5 mg/dL, 25.3±5.6 mg/dL, and 75.5±15.6 mg/dL, respectively. Mean serum CRP levels were significantly higher in patients with successful pleurodesis compared with unsuccessful patients (baseline: 4.5±3.5 mg/dL & 4.4±2.5 mg/dL; at 24h: 25.3±5.6 mg/dL & 6.5±3.5 mg/dL; at 72h: 75.5±15.6 mg/dL & 8.7±4.6 mg/dL, respectively) (p < 0.001). Complications were not serious, and the most common side effects included fever (20%) and chest pain (40%). Patients with complications had a tendency to higher serum CRP levels at the 72nd h (75.5 mg/dL & 72.7 mg/dL), but this was not statistically significant (p=0.143).

**Conclusion:** The inflammatory response in the pleural cavity due to talc pleurodesis is reflected in the systemic circulation, and high serum CRP after chemical pleurodesis, is a good predictor of the success in pleurodesis.

**P4633 Clinical characteristics, treatment and survival outcomes in malignant mesothelioma**

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**Objective:** We aimed to evaluate the clinical, radiological and survival features of patients with MM.

**Methods:** The study included 228 patients who were followed up in our center between 1993 and 2010 with the diagnosis of MM.

**Results:** The mean age was 59.1 years in men and 58.7 years in women (male/female=1.4). Environmental asbestos exposure was present in 86% of the patients for a mean duration of 40±20 years. Closed pleural needle biopsy was the most common diagnostic procedure (56.4%). One hundred-thirteen (66%) patients were treated with platinum-based combination chemotherapy (PBCT) plus supportive care (SC) and 67 (34%) patients received SC alone.

The median follow-up time was 10.0 months. The median overall survival was significantly improved with PBCT plus SC compared to SC alone (11.4 vs. 5.1 months; p=0.005). The 6, 12, 18, and 24-month survival rates were significantly improved with PBCT plus SC compared to SC alone (72%, 43%, 19%, and 2% vs. 49%, 31%, 11%, and 1%).

**Conclusion:** The survival of patients with MM improved in patients treated with PBCT. The survival advantage continued 12- and 24-month after the initial time of combination chemotherapy.

**Abstract printing supported by Chiesi Visit Chiesi at Stand B2.10**