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PRIMARY CHEST HODGKIN'S DISEASE DIAGNOSED BY PLEURAL BIOPSY: CASE REPORT

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PRIMARY CHEST HODGKIN'S DISEASE DIAGNOSED BY PLEURAL BIOPSY: CASE REPORT

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SUMMARY

Hodgkin's disease involving the lung and pleura is rare. A case of a 40-year-old woman with one year history of pain in the left arms spreading into chest is presented. Computed tomography showed a mass of 5 x 7 cm in the left hemithorax mediastinum and pleura, pleural effusion and mediastinal lymphadenopathy. Diagnostic methods including percutaneous needle aspiration biopsy of pleura, bronchoscopic biopsies, bronchoalveolar lavage, cytological examination of the pleural fluid did not disclose any pathological diagnosis. Lastly, we performed pleural biopsy by video-assisted thoracoscopic surgery and we showed that the lesion was HD of nodular sclerosing type.

INTRODUCTION

Hodgkin disease (HD) is a rare disorder and account for about 1% of cancer annually in Western countries(2). HD is more prevalent in males and there is bimodality in the incidence of HD with an initial peak in young adults and a second peak after 50 years of age(1,2).

Pulmonary involvement occurs in slightly more than 10% of patients and is virtually always associated with mediastinal node involvement(3). However, lung involvement is reported to be 38% in some other resources(5). Nodular sclerosing HD is the most common histologic type in 67% to 89% of patients having thoracic involvement(3). There is no report about the frequency of pleural involvement in HD.

Video-assisted thoracoscopic surgery (VATS) has recently been applied to diagnose and treat a variety of thoracic diseases. This technique is simpler and easier than conventional thoracotomy and has been proved to be an effective procedure. VATS is especially used in the following situations: undiagnosed pleural effusion, recurrent pneumothorax or bullous lung disease, stage II thoracic empyema, lung cancer staging, peripheral pulmonary nodule and wedge biopsy for diffuse lung disease. VATS may be performed with only regional anaesthesia and intravenous sedation. Only an incision of one centimeter is made as if one were inserting a chest tube. VATS may be performed with a shorter operation time compared to conventional thoracotomy. There are significantly less complications in the VATS group. Most

of the complications are either prolonged air leakage or supraventricular dysrhythmias.

We present a case of HD diagnosed by VATS since we could not find any other such case in the MEDLINE.

CASE REPORT

A forty-year old woman, a passive smoker, admitted to hospital with one year history of pain in the left arm that spread into chest. Four months prior to this evaluation, she had a productive cough, sputum, dyspnoea, night sweats, malaise and unexplained loss of 20 kg in body weight.

On physical examination, the temperature was 37.8°C with normal vital signs, no peripheral lymph nodes were detected. Chest auscultation noted a decrease in breath sounds. Other systems revealed no abnormalities. Laboratory results showed raised erythrocyte sedimentation rate (ESR) of 78 mmh⁻¹, white blood cell (WBC) count of 10,000/mm³, platelet count of 410,000 mm³, haemoglobin (Hb) of 11.3 g/dl and haematocrit (Htc) of 36%. Peripheral blood smear disclosed: Neutrophils (69%), bands 13%, monocytes 4%, lymphocytes 14%. Erythrocyte morphology was normal. Purified protein derivative (~mantoux test) was negative. β₂-microglobulin was 3737 µg/ml (reference range: 1010-1790) and lactate dehydrogenase (LDH) was 548 U/L (reference range: 230-460). Abdominal ultrasonography and bone marrow biopsy did not reveal any pathological findings.

Chest x-ray showed pneumonic-alveolar pattern of infiltration and small effusion in left hemithorax (Figure 1). Computed tomography scanning revealed a mass of 5 x 7 cm in the left hemithorax, mediastinum and pleura; peribronchial and perivascular thickening, alveolar-interstitial infiltrates and mediastinal lymphadenopathy (Figure 2).

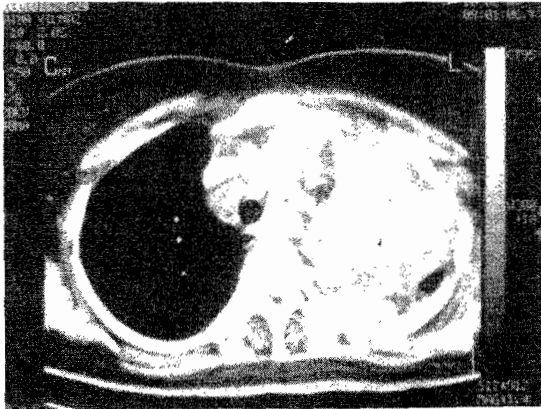
Figure 1

Posteroanterior chest radiograph of the patient



Figure 2

Computed tomograph of the patient



Percutaneous needle aspiration biopsy and bronchoscopic biopsy performed two times did not procure diagnostic specimen or uncover any pathological diagnosis. Bronchoalveolar lavage (BAL) did not disclose any malignant cells. Cytological examination of the pleural fluid did not reveal any diagnosis either. Pleural needle biopsy was performed by VATS. Examination of the biopsy material confirmed the clinical impression of HD.

Figure 3

Obvious modularity (H.E. $\times 90$)

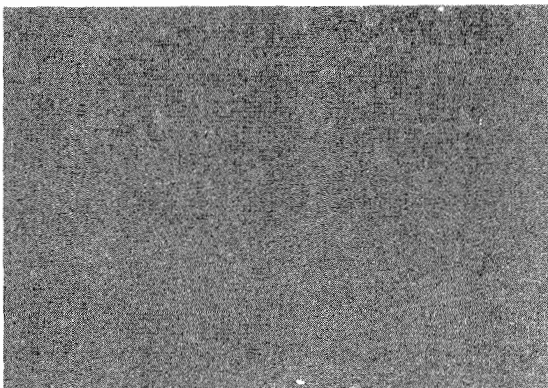
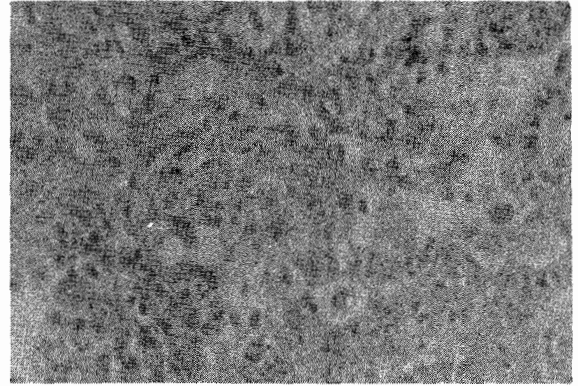


Figure 4

Lacunar cell in cellular nodular



Grossly, the parietal pleura was unevenly thickened. Low-power microscopy revealed cellular nodules separated by broad bands of fibrous tissue (Figure 3). Higher magnification showed a cell population composed of numerous lacunar Reed-Sternberg cells, mononuclear Hodgkin cells, cells with multilobated nuclei, lymphocytes, histiocytes, plasma cells and eosinophils (Figure 4).

ABVD regimen was started (adriamycin 25 mg/m² iv, Bleomycin 10 mg/m² iv, Vinblastin 6 mg/m² iv, DTIC 3755 mg/m² iv). After two cycles of this treatment her symptoms disappeared. After three cycles of the regimen, her x-ray and CT findings showed significant regression. At the end of six cycles of treatment she was in complete remission and we planned to follow her every two months.

DISCUSSION

HD with lung as the primary lesion is quite rare(3,6). In a retrospective study of 624 patients, Cionini *et al* (7), found that feminine sex, nodular sclerosing type, presence of constitutional symptoms and age younger than 36 years were more frequent in patients with mediastinal lymphadenopathy compared to patient with a normal mediastinum. In different series, nodular sclerosing histology is the presenting type in 67-84% of cases having thoracic involvement(3). Pleural effusion, developing as a result of lymphatic obstruction or pleural involvement, is found in 16% of patients(5). Histological type, clinical and roentgenographic features of our patient were in accordance with other findings in literature.

In HD, systemic symptoms were fever, weight loss and malaise(2,8). Cough and dyspnoea are observed if there exists pulmonary and/or mediastinal and/or pleural lesion(8). In our case, cough, sputum and dyspnoea were present in addition to the other systemic symptoms. After non-specific antibiotic treatment her sputum disappeared. She continued to have non-productive cough and the chest x-ray did not show any change.

The most frequent finding in lymphoma observed in lung parenchyma is mass or mass like lesions(9). The other features in thoracic computed tomography were

nodules less than 1 cm, alveolar or interstitial infiltrates, masses of pleural origin, peribronchial or perivascular thickening, pleural effusions and hilar or mediastinal lymphadenopathy(9). In two-thirds of the cases, more than one computed tomography findings were detected(9). We observed that six of these computed tomography features were present in our patient.

The paranchymal involvement of the disease should be distinguished from the infectious disease(3). Our patient was treated with antibiotics, and roentgenographical finding did not change. In conclusion, alveolarinterstitial infiltrates in our patient was due to HD. Intrathorasic HD may be diagnosed by different methods. Demonstration of typical Reed-Sternberg cells may be done using material from bronchoalveolar lavage, endobronchial brushing, sputum cytology, fine needle aspirate, closed pleural biopsy, transbronchial biopsy or open lung biopsy. There is no report comparing the efficiency of these different techniques(3). In our case, the diagnosis was made by the pathological examination of pleural biopsy obtained by VATS.

VATS has advantages over percutaneous pleural biopsy, and is an excellent diagnostic tool to confirm tissue diagnosis in patients with undiagnosed chest disease (10). VATS can be used in the diagnosis and treatment of the pleura, lung, mediastinum, great vessels, pericardium and oesophagus(11). The procedure is associated with minimal morbidity, short hospital stay, better cosmetic results, less postoperative pain and less operative trauma, compared to conventional thoracotomy(11). To our knowledge, our

case is the first reported HD diagnosed by VATS pleural biopsy. We suggest that pleural biopsy by VATS should be added to the list of diagnostic techniques of thoracic HD before consideration of more invasive methods.

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NEW PRODUCT ANNOUNCEMENT

Pfizer Laboratories Limited is pleased to announce the availability in Kenya of LIPITOR™ (atorvastatin), a new statin therapy.

Mechanism of action: LIPITOR™ is a selective, competitive and potent inhibitor of HMG-CoA reductase, an enzyme that mediates the synthesis of sterols, including cholesterol. The primary site of action of LIPITOR™ is the liver, which is also the principal site of cholesterol synthesis and low-density lipoprotein (LDL) cholesterol clearance. Pharmacological inhibition of HMG-CoA reductase by LIPITOR™ reduces intracellular cholesterol production. This leads to compensatory increase in the activity of LDL cholesterol receptors in the cell-surface of liver cells, providing for enhanced hepatic removal and catabolism of circulating LDL cholesterol.

LIPITOR™ reduces plasma total cholesterol, LDL cholesterol and apolipoprotein (apo) B in patients with homozygous and heterozygous familial hypercholesterolaemia, non-familial (secondary) forms of hypercholesterolaemia and mixed dyslipidaemias.

Pharmacokinetics and metabolism: Following oral administration, LIPITOR™ is rapidly absorbed with maximum concentration achieved in one to two hours with 95% to 99% bioavailability. Absolute bioavailability of LIPITOR™ (the parent drug) is approximately 12%; systemic availability of HMG-CoA reductase inhibitory activity is about 30%. The low systemic availability of LIPITOR™ is attributed to pre-systemic clearance in gastrointestinal mucosa and/or hepatic first-pass metabolism. Although food decreases the rate (25%) and extent (9%) of drug absorption as assessed by C_{max} and Area Under Curve (AUC), the reduction of LDL cholesterol is similar whether LIPITOR™ is given with or without food. LIPITOR™ can be administered at any time of the day.

LIPITOR™ is 98% or more bound to plasma proteins. It is extensively metabolised by cytochrome p450 3A4 to ortho- and parahydroxylated derivatives and; approximately 70% of circulating inhibitory activity for HMG-CoA reductase is attributed to active metabolites.

LIPITOR™ and its metabolites are eliminated primarily in the bile. Mean plasma elimination half-life of LIPITOR™ (parent substance) is 14 hours, but the half-life of inhibitory activity for HMG-CoA reductase is 20 to 30 hours due to the contribution of active metabolites. Less than two per cent of a dose of LIPITOR™ is recovered in urine after oral administration.

Efficacy: In a dose-response trial, LIPITOR™ provided dramatic reductions in LDL cholesterol of 41% to 61% across the dosage range of 10 mg to 80mg daily(1). At the starting dose of 10 mg daily, LIPITOR™ lowered total cholesterol, LDL cholesterol and triglycerides in hypercholesterolaemic patients significantly more than the starting doses of simvastatin, pravastatin or fluvastatin (2,3).

LIPITOR™ is indicated to reduce both elevated LDL cholesterol and triglycerides in patients with high cholesterol, making it an appropriate therapy for a broad range of patients.

Indications and dosage: LIPITOR™ is indicated as an adjunct to diet to reduce elevated total cholesterol, LDL cholesterol, apolipoprotein-B, and triglyceride levels in patients with primary hypercholesterolaemia (heterozygous familial and non-familial) and mixed dyslipidaemias.

LIPITOR™ indications:

- Reduce elevated total cholesterol, LDL cholesterol, apo B, and triglycerides in
 - primary hypercholesterolaemia
 - mixed dyslipidaemias
 - heterozygous familial hypercholesterolaemia
- Reduce elevated total cholesterol and LDL cholesterol in:
 - homozygous familial hypercholesterolaemia (as adjunct to other lipid-lowering modalities).

All patients should be placed on a lipid-lowering diet before initiation of LIPITOR™ therapy. The recommended starting dose is LIPITOR™ 10 mg once daily, and the dose range is 10 mg to 40mg once daily. LIPITOR™ is given as a single dose at any time of the day. After initiation and/or upon titration of the dose, lipid levels should be analysed within two to four weeks and dosage adjustments should only be made after an interval of four weeks or more.

Therapeutic effect is observed within two weeks; with a maximum response observed within four weeks. Renal disease does not affect the plasma concentrations or LDL cholesterol reductions of LIPITOR™ and, thus dosage adjustment is not required in patients with renal impairment.

Safety: LIPITOR™ is generally well tolerated. In head-to-head clinical trials, LIPITOR™ provided discontinuation rates comparable with other statins(4). In patients participating in controlled clinical trials, the most commonly reported adverse events were diarrhoea, constipation, flatulence, dyspepsia, abdominal pain, headache, nausea, myalgia, arthralgia, asthenia, insomnia and rash(4).

Availability and packaging: LIPITOR™ is available as 10 mg and 20 mg, white elliptical, film-coated tablets embossed "10" on one side and "PD 155" on the other side for the 10 mg tablet and "20" on one side and "PD 156" on the other side for the 20 mg tablet. LIPITOR™ 10 mg and 20mg are both available in blister packs of 28 tablets.

Product information: Full Lipitor™ information is available on request from:



Pfizer Laboratories Limited,
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Fax: 254 (2) 531 207

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