Metastatic Carcinoma of Unknown Primary Presenting as Pleural Effusion

Rajmadhangi D [*], Swathy moorthy [**], Ramakrishnan S R [**]

[*] Department of General Medicine, Sri Ramachandra Medical College Hospital and Research Centre, No.1, Ramachandra Nagar, Porur, Chennai-600116,Tamil Nadu, India.

Abstract- A **65-year-old female** patient presented with unilateral massive pleural effusion. CECT abdomen and thorax revealed features suggestive of pleural, lung, parenchymal, liver and peritoneal metastasis. Despite intensive investigation primary could not be identified. Histopathology and immunohistochemistry examination narrowed down the possibilities of the metastatic carcinoma of unknown primary.

Index Terms- Metastatic carcinoma – Unknown primary – Immuohistochemistry.

I. INTRODUCTION

In male patients about 50% of malignant effusions are caused by lung cancer, 20% by lymphomas or leukemia, 7% from gastrointestinal primaries, 6% from genitourinary primaries, and 11% from tumors of unknown primary site. In female patients, about 40% of malignant effusions are caused by breast cancer, 20% from tumors arising in the female genital tract, 15% from lung cancer, 8% from lymphomas or leukemia, 4% from gastrointestinal tract primaries, 3% from melanoma, and 9% from tumors of unknown primary site [1].

Here we present a rare case of unilateral malignant pleural effusion, which was due to metastatic carcinoma of unknown primary.

II. CASE REPORT

A 65-year old female patient presented to us with shortness of breath for the last 1 month. There was no history of fever, cough, chest pain, haemoptysis, abdominal pain, vomiting or loss of appetite and weight. Past history of hysterectomy for fibroid uterus 25 years back. There was no pallor, icterus, lymphadenopathy, clubbing, or pedal edema. Air entry was decreased in the left inframammary and infrascapular regions. The cardiovascular system and gastrointestinal system were normal. The complete blood cell count, blood sugar, renal function test and liver function test were all found to be within normal ranges. A posterior to anterior (PA) view chest X-ray was done which showed homogenous opacity in the left lower lung field along with blunting of left costophrenic angles with mediastinal shift to right suggestive of left massive pleural effusion.

Examination of pleural fluid showed its exudative nature; ADA, culture and malignant cells being negative. An ultrasound of the abdomen and pelvis detected large heterogeneous mass lesion of size 8.7x 7.o cm in the left lobe of liver and massive left pleural effusion. Above features raised possibilities of primary Hepatocellular carcinoma or liver metastasis. A contrast-enhanced computed tomography (CECT) scan of the thorax and abdomen revealed heterogeneously enhancing irregular mass lesion in segment 4 A, 5B and 5 of liver (Fig 1) extending to the surface with irregular border multiple enlarged periportal lymph nodes, thickening of omentum with nodular appearance with small amount of ascites. Multiloculated gross left pleural effusion with nodular thickening along the pleura with multiple scattered right lung parenchymal nodules (Fig. 2). The ovaries appeared normal and no other mass lesion was detected A test for cancer antigen 125 (CA 125) showed that the level of CA 125 was elevated (410 U/ml), but carcinoembryonic antigen (CEA); alpha feto protein (AFP); CA19.9 was negative. A histologic examination of the USG guided biopsy of the liver lesion showed dense areas of fibro collagenous tissue infiltrated by few clusters of cells with moderate pleomorphism and nuclear hyperchromasia Fig3.

Immunohistochemistry was positive for Vimentin and Cytokeratin 7 but negative for Cytokeratin 20, Synaptophysin, TTF1, and Glypican. Above feature suggested possibilities of Ovary non mucinous; Thyroid; Breast; Lung; Mesothelioma; Cholangio carcinoma. A gynecological examination did not reveal any abnormality. An upper gastrointestinal endoscopy and colonoscopy did not show any abnormal lesion. A breast examination was normal. Examinations of the oral cavity and indirect laryngoscopy were also with a diagnosis of metastatic carcinoma of unknown primary; she was referred to the oncology department. She showed an initial response to cisplatin and paclitaxel and remained well at 2 months follow-up.

III. DISCUSSION

Even with an extensive diagnostic work-up using modern pathological and imaging procedures, the frequency of detection of the primary tumor site remains low. Less than 20% of patients have a primary site identified ante mortem, while from necropsy data it was found that almost 70% of autopsied cases remained undiagnosed. Post-mortem detection of a primary site may be higher in patients with well-differentiated adenocarcinomas [2,3]. Ultimately, primary sites are most frequently detected in the lung and pancreas, followed by other gastrointestinal and gynecological malignancies. In general, it appears that patients with CUP have a limited life expectancy with a median survival of ~6–9 months. However, some subsets have a better prognosis and enjoy longer survival. Analyses of prognostic and predictive factors in CUP have examined several clinicopathological

parameters. Several positive and negative prognostic and predictive factors were detected, which helped to define several favorable and unfavorable groups of CUP patients.

Immunohistochemical studies sometimes result in the identification of tumor origin, especially if the metastases are poorly differentiated by light microscopy. Several cell components can be identified by a series of monoclonal or polyclonal immuno- peroxidase antibodies including enzymes, structural tissue components, hormonal receptors, hormones, oncofetal antigens or other substances [3]

The development of monoclonal antibodies against various cytokeratin (CK) polypeptides has opened new avenues in investigating the normal and cancerous epithelial cells. Among them, CK7 and CK20 have been extensively studied in solid tumors. CK20 appears to be very useful in diagnosing gastrointestinal adenocarcinomas, while CK7 is more common in respiratory or gynecological malignancies [3].

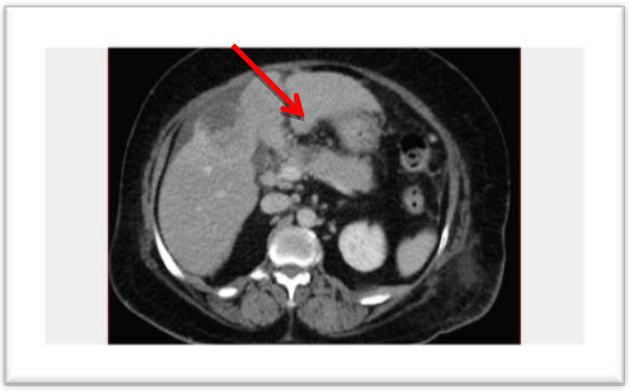

Fig 1. LIVER LESION

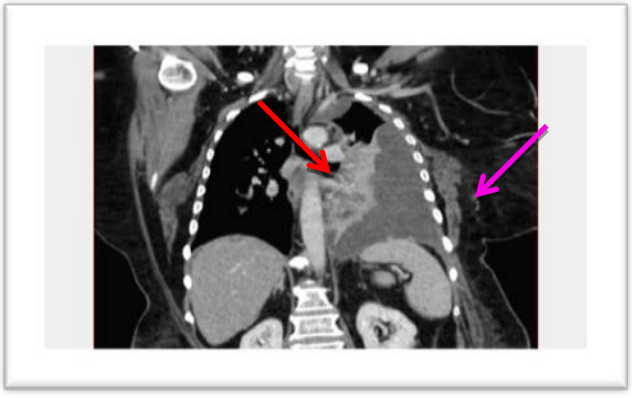

Fig 2. GROSS LEFT PLEURAL EFFUSION WITH NODULAR PLEURAL THICKENING (pink arrow) AND PARENCHYMAL METS (red arrow)

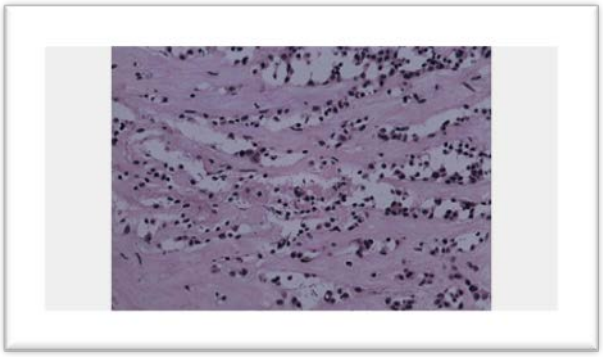

Fig 3. USG guided biopsy of the liver lesion showed dense areas of fibro collagenous tissue infiltrated by few clusters of cells with moderate pleomorphism and nuclear hyperchromasia

IV. CONCLUSION

Metastatic carcinoma of unknown primary may rarely present as pleural effusion. Hence it should be evaluated with higher imaging modalities in suspected patients even if pleural fluid is negative for malignant cells. Immunohistochemistry markers; especially, cytokeratins are useful in narrowing down the possibilities for unknown primary malignancies for starting an empirical chemotherapy.

REFERENCES

[1] Johnston WW. The malignant pleural effusion: a review of cytopathologic diagnoses of 584 specimens from 472 consecutive patients. Cancer. 1985; 56(4): 905–909. [PubMed]

[2] Briasoulis E, Pavlidis N. Cancer of unknown primary origin. Oncologist 1997; 2: 142–152.

[3] Pavlidis N, Briasoulis E, Hainsworth J, Greco FA. Diagnostic and therapeutic management of cancer of unknown primary. Eur J Cancer 2003; In press.

AUTHORS

First Author – Rajmadhangi. D, MBBS, Postgraduate resident, SRMC medical college hospital and research centre, mathurockz@yahoo.co.in.
Second Author –Swathy Moorthy MD Geeneral Medicine, Assistant professor, SRMC medical college hospital and research centre.
Third Author –Ramakrishnan S R Professor, SRMC medical college hospital and research centre.

Correspondence Author – Rajmadhangi. D, MBBS, Postgraduate resident, SRMC medical college hospital and research centre, mathurockz@yahoo.co.in. contact no: +91 9894662333