DIAGNOSIS OF UNDIFFERENTIATED CARCINOMA WITH THE HELP OF MONOCLONAL ANTIBODIES

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INTRODUCTION

Undifferentiated carcinomas and malignancy of unknown origin (MUO) present one of the greatest challenges to the pathologist as well as oncologist.[1] Without knowing the primary or the type of primary tumour, it becomes very difficult for the oncologist to plan treatment for the patient. Despite exhaustive investigations, 5% of all cancer patients (and 70% of MUOs) will still have an unidentified primary tumour.[2] Due to this high rate of failure to identify the primary or the type of primary tumour, coupled with the fact that prognosis is very poor in these patients, one should only try to eliminate the most treatable tumours (e.g. breast, ovarian, testicular carcinomas).[3] Men with tumours of undifferentiated histology should have screening for human chorionic gonadotrophin (hCG) and alpha-feto protein (AFP), specially if they have features of extra-gonadal tumours.[4,5] The advent of monoclonal antibodies (Mabs) and the production of a battery of Mabs to various tumour associated antigens has helped alot in diagnosing certain malignancies of undifferentiated histology or of unknown origin.[6] These Mabs are increasingly being used in most well-equipped laboratories world wide on frozen sections for the diagnosis of such tumours. MUOs or undifferentiated carcinomas are not uncommon in Pakistan and we come across quite a few patients who have either undifferentiated carcinoma or MUO. Identifying the primary tumour is very tedious, time consuming and expensive. With the introduction of monoclonal antibodies in Pakistan, hopefully, diagnosing such cases will become easier.

Here we describe a case which was reported as undifferentiated carcinoma initially. Mabs were used on paraffin sections of the tumour to determine the exact nature of the primary tumor which led to its proper diagnosis and treatment.

CASE REPORT

A 50 years old man presented to Male Surgical A Ward of Lady Reading Hospital, Peshawar, with complaints of pain in the right hypochondrium and fever. A laparotomy was performed and biopsy was taken from the mass. Due to extensive involvement of the arteries and other structures, the mass could not be excised. During laparotomy, para-aortic nodes were also palpable and liver had course architecture.

Blood count, blood urea, creatinine, electrolytes and LFTs were all within

normal range. His M.P. and Widal tests were negative. Blood film for malarial parasite Alpha feto protein (AFP) was >350 ng/ml (normal range 0-10 ng/ml and HCG was 0.04 mlU/ml (normal range <5 mlU/ml. X-ray chest showed two well-defined rounded opacities in the right lung, approximately 2x2 cm in diameter (Fig.1).

Abdominal ultrasound showed an 11x11.5x8 cm heterogenous mass postero-medial to the right kidney, pushing the kidney anteriorly. Enlarged para-aortic nodes (1.3cm to 6.6cm in diameter) were also noted with evidence of caseation in one node. There was a 5 cm mass in postero-superior part of the right lobe of the liver. Spleen was mildly enlarged and there was no free fluid in the peritoneal cavity. There was moderate quantity of fluid in the scrotal cavity surrounding the testes, more on the right side. Both testes were reported as normal.

C.T. scan of abdomen also showed a complex mass (approximately 11x11 cm) postero-medial to the right kidney (Fig 2). Biopsy reports from various Pathologists/ Pathology Departments were as under.

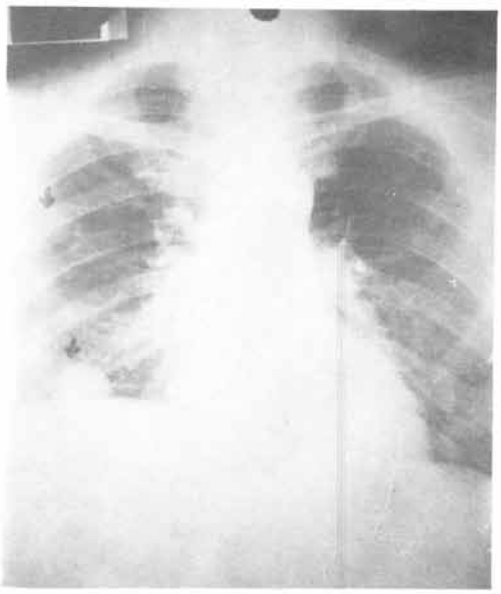

Fig. 1. Well-defined opacities seen in right lung (metastases).

Pathologist at Peshawar reported the tumor to be undifferentiated carcinoma. Second opinion from Armed Forces Institute of Pathology (AFIP), Rawalpindi, suggested the neoplasm to be pleomorphic rhabdomyo-sarcoma (RMS). Pathologist at Shifa International Hospital, Islamabad, reported the tumour to be undifferentiated neoplasm suggestive of embryonal cell carcinoma.

Due to the differing reports of various Pathologists, we decided to send the tumor specimen to Aga Khan Hospital, Karachi, for immunohistochemical staining with Mabs to reach a proper diagnosis. Immunohistochemistry report from Aga Khan Hospital is as under.

Sections of tumour were stained with the following monoclonal antibodies using PAP technique (staining report in brackets).

AFP (positive); CK (MNF) (positive), placental alkaline phosphatase (negative) HCG (negative) and vimentin (negative). Comments: Immunohistochemical features are in favor of non-seminomatous germ cell tumor. Final diagnosis: Extra-gonadal germ cell tumor (metastatic).

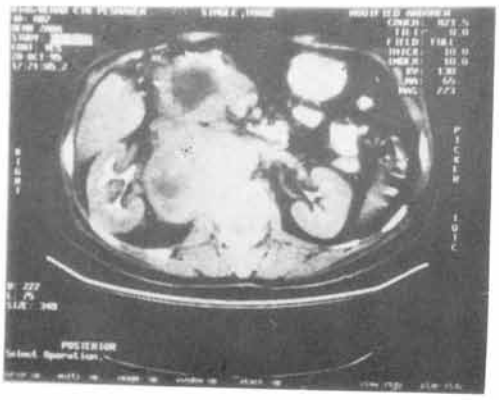

Fig. 2. C.T. scan abdomen showing a retroperitoneal mass.

Treatment: He was started on PEB regime for germ cell tumors as follows: He received four courses each extending for 03 weeks.

Inj. Bleomycin 30mg/day, IV, days 2,9,15.

Inj. Etoposide 100mg/m2 IV x 5 days

Inj. Cisplatin 20mg/m2 IV x 5 days.

DISCUSSION

Malignant tumours have been found to produce abnormal proteins and enzymes. Various groups have succeeded in raising antibodies specific for such proteins.[6] Mabs are revolutionizing the diagnosis and treatment of many malignancies. By using the specific antibodies, not only the presence of specific malignancy can be ascertained but the site of malignancy can also be detected.

The case presented here was diagnosed as undifferentiated carcinoma first and then as pleomorphic rhabdomyosarcoma (RMS). In other studies as well, many sarcomas originally diagnosed as pleomorphic RMS were later re-classified as other types of sarcomas or tumours.[7] Differentiation of pleomorphic RMS from other sarcomas/ tumors can be aided by immunohistochemical staining using antibodies specific to the constituent proteins of these tumors. In our case, a panel of antibodies including Mabs to AFP, hCG, placental alkaline phosphatase, vimentin etc. were used to ascertain the exact nature of the tumor in order to plan proper treatment. The sections of the tumor were stained with various Mabs described above and were found positive for AFP and CK (MNF), thus confirming the diagnosis of extra-gonadal germ cell tumor (embryonal cell carcinoma). Once the nature of primary tumor was confirmed, treatment was started for the disease with a good response shown by the patient. His pulmonary metastases have disappeared (Fig 3) and his primary tumor has shrunk. Embryonal cell carcinoma (ECC) is a highly

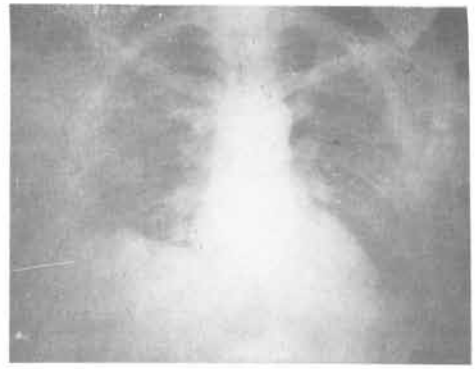

Fig. 3. X-ray chest after chemotherapy showing clearance of metastases.

malignant appearing tumor with anaplastic embryonic features. The adult form has highly variable histologic picture. AFP levels are raised in these tumors and raised levels of AFP in patient with MUO or undifferentiated carcinoma should raise suspicion of germ cell tumor/ECC. Monoclonal antibodies specific for these proteins can then be used on tissue sections to confirm the diagnosis. Although AFP can be raised in many diseases, it is specifically helpful in the diagnosis of liver cancer and germ cell tumours.[8] These extragondal germ cell tumours are highly resistant to chemotherapy but PEB regime used for testicular germ cell tumors also induces remission in these patients.

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