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Short Communication

Pathology Section

Immunohistochemistry: Illuminating and Misleading Two Oncology Cases Underscoring the Importance of Case Based Appropriate Immunomarker Selection

SARBASHIS HOTA[1], SRABANI CHAKRABARTI[2], SUBHAJIT HAJRA[3], DIPKANA DAS[4]

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ABSTRACT

Arrival of immunohistochemistry in the domain of Oncology has revolutionised our approach towards diagnosis as well as in therapeutic decision making. Here, the authors will like to discuss two interesting cases (53-year-old female and 26-year-old male) encountered in the Institution where immunohistochemistry came out to be instrumental in clinching the proper diagnosis. The second case also highlights how misleading it can be, if not applied in appropriate clinical context and without being fully coherent with immunophenotypical spectrum of commonly encountered tumours.

Keywords: Anaplastic large cell lymphoma, Invasive breast carcinoma, Metastatic discordance, Squamous cell carcinoma

INTRODUCTION

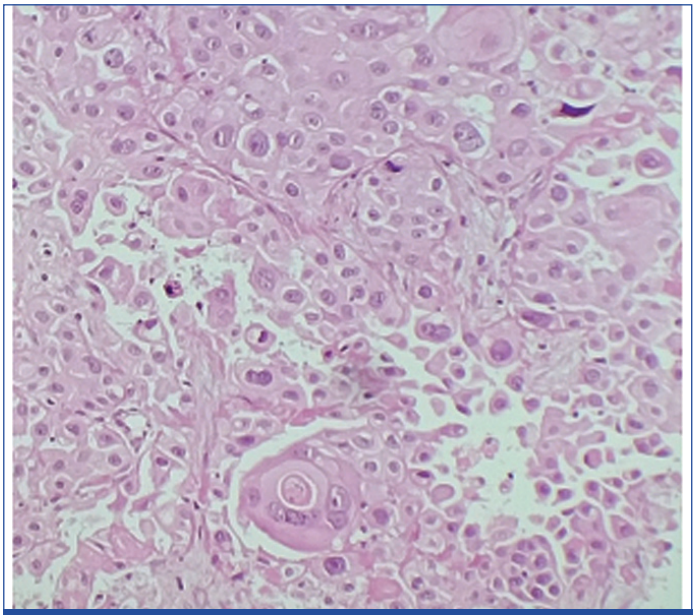
Arrival of Immunohistochemistry (IHC) in the domain of oncology has revolutionised Approach of Healthcare professionals towards diagnosis as well as in therapeutic decision making. It is obvious that like any other sophisticated tests IHC needs stringent quality control. Here, the authors will like to discuss two interesting cases encountered in the Institution where IHC came out to be instrumental in clinching the proper diagnosis. In the first case, a case morphologically presenting with features of Squamous Cell Carcinoma (SCC) involving lung, was finally diagnosed as metastatic deposit of invasive breast carcinoma with squamous differentiation. The second case was diagnosed as Anaplastic Lymphoma Kinase (ALK) positive anaplastic large cell lymphoma, which was misdiagnosed outside as rhabdoid tumour after using an exhaustive panel of IHC.This case also highlights how misleading IHC can be, if not applied in appropriate clinical context and without being fully coherent with immunophenotypical spectrum of commonly encountered tumours.

CASE REPORT

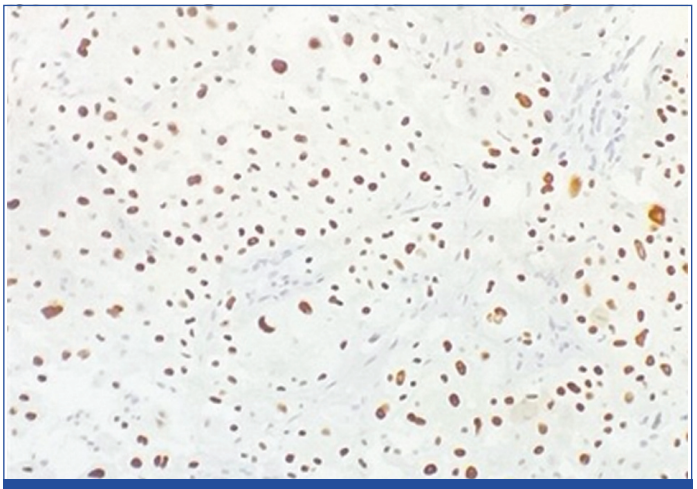
Case 1

A Computed Tomography (CT) guided core biopsy of lung from a 53-year-old lady was sent to histopathology department, without any clinical history. The morphology was that of classical squamous cell carcinoma [Table/Fig-1], diffusely positive for p40 [Table/Fig-2] and negative for TTF-1 and Napsin A. However, the matter became complicated with evaluation of radiology which showed multiple cannon ball metastasis involving both lung fields. Now, it was more in favour of secondaries with primary SCC elsewhere in the body. But to complicate the matter further, Positron Emission Tomography-Computed Tomography (PET-CT) revealed no other metabolically active focus later on.

On further interrogation, patient was found to be a case of Invasive breast carcinoma, no special type, who underwent mastectomy one year back post neo adjuvant chemotherapy and received six cycles of adjuvant chemotherapy afterwards. Even if the previous history of breast cancer would have known beforehand, it would



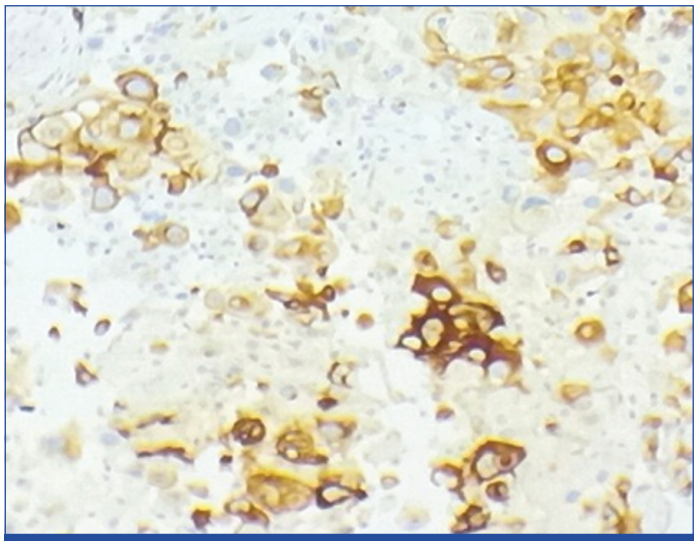
[Table/Fig-1]: Core biopsy lung mass, Haematoxilin and Eosin (H&E), 100X.



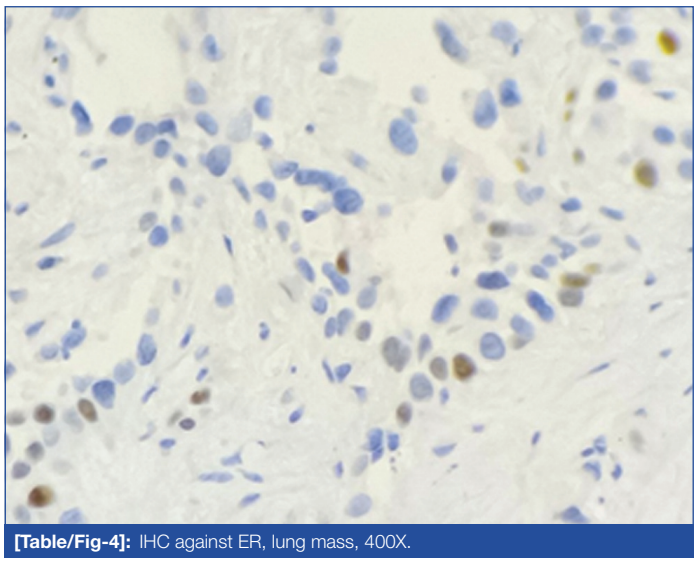
[Table/Fig-2]: IHC against p40, lung mass, 400X.

be problematic to think this case as a metastasis with such florid squamous differentiation, which will otherwise clearly indicate towards squamous cell carcinoma, particularly when the previous diagnosis was invasive breast carcinoma, no special type; not that of a metaplastic carcinoma of breast.

So, on remote suspicion, an immunopanel of Epithelial Membrane Antigen (EMA), GATA3 and Gross Cystic Disease Fluid Protein -15 (GCDFP-15) [Table/Fig-3] were run, strikingly all three came out to be positive. The lung tumour also showed focal but strong expression of Estrogen Receptor (ER) [Table/Fig-4]. On review of previous slides, few areas of squamoid differentiation was found in the mastectomy specimen post neo-adjuvant therapy [Table/Fig-5], which was aptly reported as Invasive Breast Carcinoma (IBC), No Special Type Bloom Richardson (NSTBR) grade 3;- florid squamous differentiation that will otherwise stand for metaplastic carcinoma was not present in the sections. No such area was apparent in the first core biopsy. When stained with antibody against p40, these foci showed strong expression.



[Table/Fig-3]: IHC against GCDFP-15, lung mass, 400X.

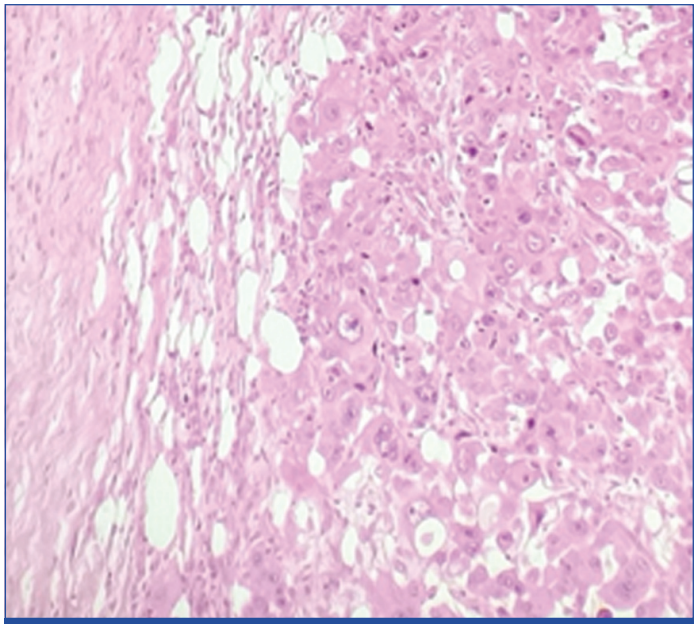


[Table/Fig-4]: IHC against ER, lung mass, 400X.

So, a final report of metastatic deposit of carcinoma with squamous differentiation, of primary breast origin was released.

Case 2

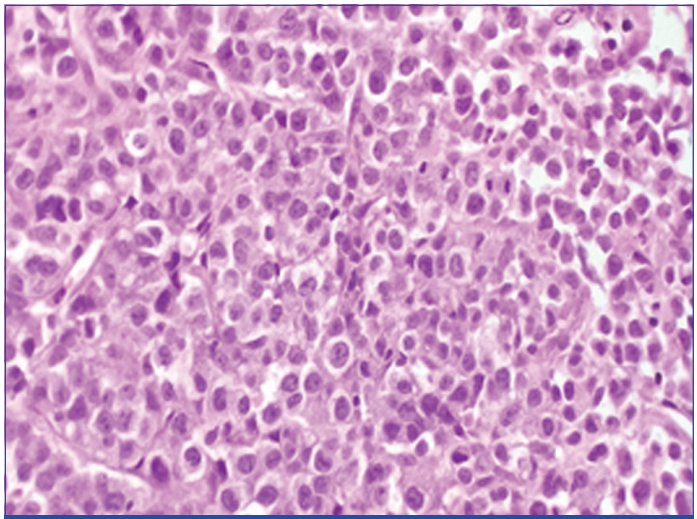
This case initially came as a review. A 26-year-old male presented with a large neck mass infiltrating the soft-tissues of neck and overlying skin associated with bilateral cervical lymphadenopathy. An Fine Needle Aspiration Cytology (FNAC), performed outside, was reported as diffuse large cell lymphoma, which was submitted for review. However, a biopsy report along with IHC also accompanied



[Table/Fig-5]: Areas of squamoid differentiation, Mastectomy specimen, H&E, 400X.

it, reported from a separate centre,the slide/block of which was not collected by patient. The histopathology report outside, based on morphological evaluation offered two differentials- a lymphoma or a rhabdomyosarcoma. The IHC report from outside incorporated 17 immunomarkers, which reported strong vimentin expression and loss of INI coupled with negative expression of desmin. A final diagnosis of extrarenal rhabdoid tumour was made at the outside centre;- CD45, CD3, CD20, CD68, S-100, MPO all were reported negative.

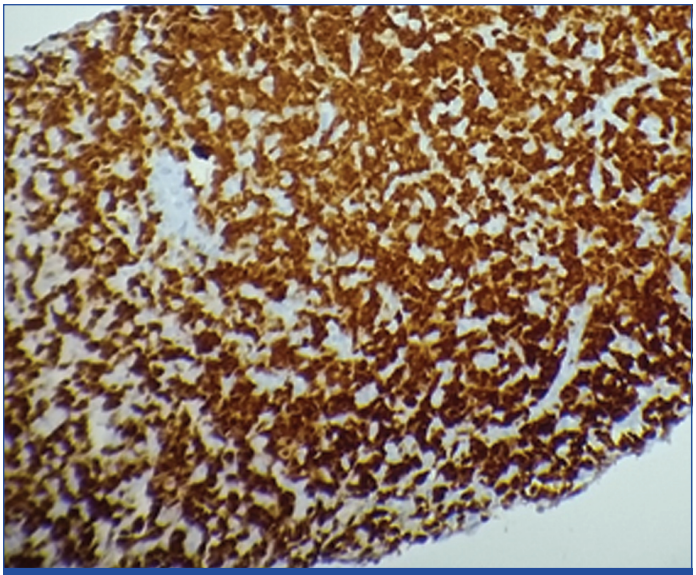
The FNAC review report was dispatched as suggestive of lymphoproliferative disorder, however, for final diagnosis, corroboration with histopathology was essential. As the tissue block was not available, an in-house core biopsy was done. The HP slide [Table/Fig-6] showed solid sheets of medium to large round atypical cells with high N:C ratio, hyperchromatic nuclei, prominent nucleoli and basophilic cytoplasm. CD45, CD3, CD20 came out to be negative however the neoplastic cells show strong diffuse expression of CD30 and EMA. IHC against ALK [Table/Fig-7] was run next, which was diffusely positive.Though hallmark cells were not quite obvious in the small core biopsy, a final diagnosis of ALK positive anaplastic large cell lymphoma was released.



[Table/Fig-6]: Core biopsy neck mass, H&E, 100X.

DISCUSSION

The GATA3 expression is rare in primary lung squamous cell carcinoma [1]. GCDFP-15 and ER expression clearly indicates towards a breast primary, especially in this context where focal



[Table/Fig-7]: IHC against ALK, neck mass, 100X.

morphological squamous differentiation was proved by IHC in the mastectomy specimen. Under the selection pressure of adjuvant chemotherapy, the clone with squamous differentiation was selected, which was able to establish a lung metastasis. This scenario is coherent with multistep tumour progression model by classical Darwinian selection [2]. Multitude of studies is available in existing literature highlighting the immunophenotypic discordance between primary and metastatic breast cancer [3,4]. Histologic discordance between primary breast cancer and nodal metastasis is also reported [5]. However, apparent drastic change of histomorphology in primary and metastatic breast cancer like this case is not reported before, as far our knowledge goes.

Anaplastic lymphoma is known to arise from extranodal sites like skin and soft-tissue along with nodal involvement. This was the situation in this context. The fallacy is that ALCL often under-expresses common T cell markers (CD3 is expressed only in 15% cases) and express EMA;-So the misdiagnosis as non haematolymphoid neoplasm is not uncommon [6]. The null phenotype of ALCL is particularly difficult to diagnose if not separately searched for. CD 30 often is an instrumental marker before completely ruling out a tumour of haematolymphoid origin, though, it is known that it may become positive in varieties of cases including germ cell tumour [7]. Not just Hodgkin lymphoma, the list of CD30 expressing lymphoma is long comprising of peripheral T cell lymphoma, EBV positive DLBCL, EBV positive mucocutaneous ulcer, Plasmablastic lymphoma, primary effusion lymphoma, Enteropathy associated T cell lymphoma, lymphomatoidpapulosis and many others.

CONCLUSION(S)

The IHC may become instrumental in appropriate diagnosis in specific clinical contexts. However, the pathologist should be well oriented with the immunotypic characteristics of normal tissue along with pattern of expression (under-expression or an aberrant one) of common pathological conditions of same histogenesis. Blind use may lead to a diagnosis, which is equally detrimental for the patient and the pathologist.

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PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of Laboratory Medicine, Chittaranjan National Cancer Institute, Kolkata, West Bengal, India.
2. Senior Consultant, Department of Laboratory Medicine, Chittaranjan National Cancer Institute, Kolkata, West Bengal, India.
3. Consultant, Department of Laboratory Medicine, Chittaranjan National Cancer Institute, Kolkata, West Bengal, India.
4. Consultant, Department of Laboratory Medicine, Chittaranjan National Cancer Institute, Kolkata, West Bengal, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Sarbashis Hota,
Raghunathpur (Opp. KKI), Jhargram, Kolkata-721507, West Bengal, India.
E-mail: sarbashishota94@gmail.com

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