Clinicopathological and Novel immunomarkers correlation in Gall bladder cancer cases and its precursor lesions

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Background: The Indian Council of Medical Research in India has reflected that the occurrence of Gall bladder carcinoma (GBC) is predominantly higher in northern India. Reports from ICMR suggests that the incidence of GBC corresponds to 3.6 per million in males and 7.4 per million in females in Delhi, India, as compared to 1.13 per million in the US. The incidence is high in females and it represent almost three fourths of GBC victims and their highest incidence rate occur in this region, yet only few immunomarker studies are available from this high-predisposing region. GBC has also been reported to show a variable expression pattern among different ethnic groups.

GBC results via the dysplasia-metaplasia sequence and the 5-year survival rate for GBC is 32% and for the advanced stage it is only 10%. Current studies have focused on the importance of Cyclin D1, E-cadherin, EGFR, HER- 2, Ki67, and p53 immunomarkers in the development and prognosis of GBC. One of the most genetic aberrations is ascribed to be HER-2 in GBC. HER-2 and other immunomarkers Cyclin D1, E-cadherin, EGFR, Ki67, and p53 can be easily assessed by standard immunohistochemistry methods. However, concrete results have not been obtained due to a limited number of respectable GBC cases presented atthe hospitals. We, therefore, attempt to evaluate the immune-expression of these markers in GBC cases and determine their prognostic value in the selected GBC cohort.

Material and Methods: 30 resected GBC cases were collected from the Gall bladder lesion cases. Histological type, and differentiation grading of all specimens was obtained from H&E-stained slides. Immunohistochemistry Formalin-fixed (10%), paraffin-embedded GBC were sectioned (3–5 µm thick) and were treated with ready-to-use monoclonal antibodies Cyclin D1, E-cadherin, EGFR, HER- 2, Ki67, and p53 c-erbB-2 of (Dako® Corporation, Carpinteria, Calif., USA) were used as the primary antibody. Scoring was based on the HerceptestTM (Dako) criteria; semi-quantitative analysis of the stain intensity was carried out.

The number of Immunomarker-stained cells in representative microscopic fields were counted and the percentage of positive cells was ad-judged as negative (0) or barely perceptible staining in <10% tumor cells (0), weak staining in <30% tumor cells (+1), strong, complete membranous staining in >30% cells (+2) while immunomarker positivity was established when more than 50% tumor cells exhibited complete nuclear staining (+3) . Statistics

Statistical analysis was performed using SPSS software 23.0. Statistical significance was set at $p < 0.05$.

Results: The average age of the patient cohort was 53 years, and 55% of them were females. 62% of cases had gallstones of different sizes and the average tumor size was 45 mm. All the cases were mostly histologically proved to be adenocarcinoma. About 11/30 of the patients showed staining for HER-2 , and 10/30 of the tumor cases showed positivity for p53,14/30 of

the tumor cases showed positivity forCyclin D1,12 /30 of the tumor cases showed positivity for E-cadherin,113 /30 of the tumor cases showed positivity for EGFR, and 17 /30 of the tumor cases showed positivity for Ki67.Contingency table analysis by χ 2 tests showed that HER-2,Cyclin D1, E-cadherin, EGFR, positivity showed significance with sex ($p = 0.02$). On the other hand, Ki67, and p53-positive cases did not show any significance with clinicopathological factors. HER-2, Cyclin D1, E-cadherin, EGFR, Ki67, and p53 showed statistical significance. Hence their expression is considered to be significant prognostic factors in the selected GBC cohort.

Conclusions: Consequently, it can be summed up that there is an important need to search for immuno- markers of GBC, which will not only diagnose and prognosticate the disease but also help in choosing the appropriate mode of therapy and may give us an opportunity to make our basic understanding of GBC pathology clearer. Furthermore, anprecise molecular categorization of GBC is necessary for the enrolment of patients in clinical trials in order to define which patient groups are likely to gain the most aimed therapy. Multiple cellular pathways influence the growth and metastatic potential of tumors creating the potential for tumors to overcome the signaling pathway blockade. Combining therapies that inhibit different intracellular signaling pathways have the potential to be more effective in overcoming tumor resistance. A new promise in gall-bladder treatment is the inhibition of the master heat shock protein 90, which has emerged as an exciting target for cancer therapy, which is a master regulator of the stability and activity of multiple oncoproteins such as HER-2, Cyclin D1, E-cadherin, EGFR, Ki67, and p53. Thus, our study assesses the expression of important immunomarkers involved in the pathogenesis of GBC, correlates it with clinicopathological parameters and establishes it as an independent prognostic factor in GBC.

Biography

Dr. Anshoo Agarwal is currently working as Professor & Chairperson at Department of Pathology, Northern Border University, Arar Kingdom of Saudi Arabia. She received her Bachelor of Medicine & Bachelor of Surgery from King George's Medical College Lucknow. Dr. Anshoo Agarwal received her M.D in Pathology from LLRM Medical College / Ch. Charan Singh University. She is an Associate professor and Discipline Coordinator in University Technology MARA, Malaysia. Dr. Anshoo Agarwal has served on many scientific memberships like Life member of Indian Association of Pathology and Microbiology, Member of International Academy Pathology, Life member of Indian Society of Hematology & Transfusion Medicine, Emirates Medical Association Pathology Society. Dr. Anshoo Agarwal has more than 80 publications. Dr. Anshoo Agarwal is editorial member of 3 journals and has many reviewed publications. Dr. Anshoo Agarwal research interests include Advance Haematology & Immunohematology, Breast cancer and Anticancer vaccines.