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To Evaluate GATA 3 Positivity in Gallbladder Adenocarcinoma

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Abstract:-
Background: GATA 3 immunostainis an important immune histo chemical stain used in surgical pathology for the detection of breast and urothelial carcinomas. In the recently published literature, GATA3 immunostain positivity has been reported in gallbladder adenocarcinoma. This study aims to evaluate GATA3 immunostain positivity in gall bladder adenocarcinoma.

Methodology: A cross-sectional observational study was done on 51 biopsy samples diagnosed with gall bladder adenocarcinomain the histopathology department of Chughtai Institute of Pathology.The study was conducted during January 2021-December 2021. Monoclonal antibody GATA3 (LOT P58312121, GeneAb) was applied by manual technique.

Results: GATA3 was applied on 51 cases of gall bladder adenocarcinoma with positive external control. The results of our study show negative GATA3immunostain expression in all cases.

Conclusion: In our study, no single case showed positivity for GATA3immunostain. Hence, our study supports that GATA3 immunostain positivity can be utilized primarily for detection of tumor of breast, urinary bladder and adnexal origin.

Keywords: Gall bladder adenocarcinoma, GATA3immunostain, breast, urothelial carcinoma, pathology

I. INTRODUCTION

Gall bladder adenocarcinoma (GBA) is the sixth most common malignancy among gastrointestinal tract (GIT) cancers [1,2,3] and the second most common GIT tumor among Pakistani women [4]. There is marked ethnic and geographical variation in GBA. It is the one of most common tumor in South East Asian countries witha female to male ratio of 3-4:1 [5].The mean age of presentation is the sixth decade of life.GBA is diagnosed late in life due to the absence of overt signs and symptoms and thus has a poor prognosis[6].The overall survival rate of GBA is poor with a mean survival time of 6 months anda 5-year survival rate of 5%[7].

GATA3 binding protein is one of the six members of the GATA family of transcription factors.It plays an important role in the maturation of T-lymphocytes[8],the development and differentiation of many tissues and cell types which includes mammary gland tissue,adipose tissue, kidney, trophoblastic tissue, salivary gland tissue[9],sympathetic nervous systemand hair follicles of the skin [10].It is a sensitive immunostain used in routine practice for workup of tumors of unknown primary mostly specified for mammary and urothelial tract malignancies[1,11]. The rest of tumors that show positivity for GATA3 immunostain are adnexal tumors, mesothelioma, salivary duct carcinoma, and paraganglioma. In the recent past study conducted by Guo et al, positivity of GATA3 immunostain in 8 (21%) cases of GBA was reported [1].The aim of our study was to evaluate GATA3immunostain expression in GBA.

II. MATERIALS AND METHODS

After approval from Institutional Review Board (Letter No. CIP/IRB/1052) this cross-sectional observational study was conducted over a period of one year(January 2021 to December 2021)at the Chughtai Institute of Pathology(CIP),Lahore Pakistan. All cases histologically diagnosed as gallbladder adenocarcinoma were included. Cases were extracted by using Nexus pro from archives of Chughtai lab. A total number of 51 cases were included. Poorly fixed specimens, non-neoplastic lesions, other tumor types and metastatic tumors were excluded from the study. All specimens were fixed in 10%formalin. After gross examination, representative sections were taken and routinely processed with paraffin embedding.GATA3immunostain ready to use (monoclonal antibody, LOT P58312121 by GeneAb) was applied using a manual technique. The results were evaluated by two histopathologists individually. The demographic and pathological parameters of GBA were also recorded alongwith GATA3 immunostain expression. Data was analyzed by using SPSS version 22(IBM Corp, Armonk, NY, USA).

III. RESULTS

The pathological features of 51 cases of gallbladder adenocarcinoma were recorded (Table1). In our study, the age range was 30-85 years. The majority of the patients were females 42 (82.4%) and 9 (17.6%) were males. In most of the cases, 35(68.6%) were diagnosed as moderately differentiated adenocarcinoma, followed by 11(21.6%) cases of poorly differentiated and 5(9.8%) cases as well-differentiated adenocarcinoma. None of the cases showed positivity for GATA3immunostain (Table 2).

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Pathological characteristics	Variables	Total (n=51) (%)
Cholelithiasis	Present	38 (74.6)
	Absent	13 (25.4)
Histological grade	Well-differentiated	5 (9.8)
	Moderately differentiated	35 (68.6)
	Poorly differentiated	11 (21.6)
Perineural invasion	Present	28 (54.9)
	Absent	23 (45.0)
Lymhovascular invasion	Present	11 (21.5)
	Absent	40 (78.4)
Pathological stage	pT1	7 (13.8)
	pT2	22 (43.1)
	pT3	18 (35.2)
	Not applicable	4 (7.9)

Table 1: Pathological characteristics of Gall bladder adenocarcinoma cases

Histological grade	No. of cases (n=51)	GATA3 immunostain expression (positive/negative)
Well-differentiated	5	Negative
Moderately differentiated	35	Negative
Poorly differentiated	11	Negative

Table 2: Expression of GATA3immunostain in GBA cases

IV. DISCUSSION

Gall bladder adenocarcinoma represents 80-95% of biliary tract cancers. In our study, the mean age of presentation was 59.51 years which is concordant with the international published data that states GBA affects majority of patients above 50 years of age [12]. The presence of gallstones is an important risk factor for developing GBA [13].In our study, 38(75.6%) cases had cholelithiasis.Perineural invasion was present in 54.9% of cases (Figure 1) andlymphovascular invasion in 21.5%of cases. The study conducted by Chijiiwa et al found perineural in 43% of cases and lymphovascular invasion in 68% of cases[14].

GATA3 is a transcription factor encoded by the GATA3 gene. The GATA3 gene is located close to the end of the short arm of chromosome 10 at position p14 and encodes a protein containing two GATA-type zinc fingers. Six GATA transcription factors are expressed by the human in a tissue-specific manner.GATA1 and GATA2 are present in hematopoietic tissue, GATA3 is expressed by many tissue types including T cells, mammary gland, kidney, urothelium, central nervous system, skin, and trophoblastic tissue[15], whereas GATA4, GATA5, and GATA6 are expressed by mesoderm and endodermal derived tissues such as the myocardium.

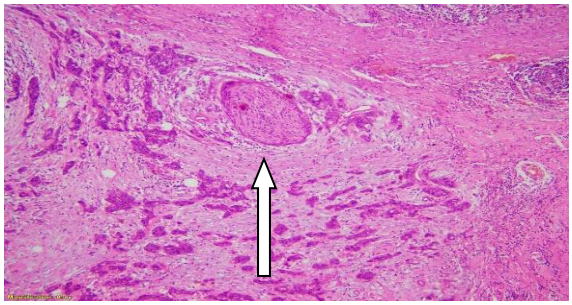

Fig. 1: Gallbladder adenocarcinoma showing perineural invasion (white arrow) x 200 H&E

In our study, we analyzed the expression of GATA3immunostain in gallbladder adenocarcinoma.Our study showed negative expression of GATA3immunostain in GBA (Figure 2). Our results were consistent with two other studies done by Higgins et al. [16] and Shield et al [17]. One study reported the positivity of GATA3 immunostain in 8 21%) cases of GBA [1] which was a significant percentage and raises the question about the use of this immunostain specified for known mammary gland, urothelial and adnexal tumors, especially in regions like Pakistan.

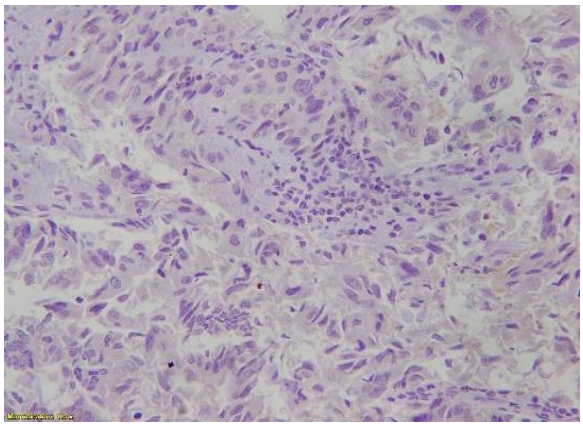

Fig. 2: Negative GATA3 immunostain expression

V. CONCLUSION

Our study showed negative GATA3 immunostain expression in gallblader adenocarcinoma. Hence, this supports the concept of using GATA3 as an adjunct for primary tumors of the breast, urothelial and adnexal tumors.

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