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Immunochemistry of skin lesions helps spot Lynch syndrome

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By David Douglas

NEW YORK (Reuters Health) - Immunohistochemical screening of sebaceous neoplasms can identify germline mismatch repair (MMR) mutations and help diagnose Lynch syndrome, according to a new paper.

The findings support recommendations for routine screening via this widely available approach, the authors say.

"Sebaceous neoplasms can be the presenting feature of Lynch syndrome, and dermatology clinics have an important role in recognizing these patients and families," lead author Jessica N. Everett told Reuters Health by email.

She added, "Our results show that a combination of detailed family history and immunohistochemistry optimizes our ability to identify patients at risk, and highlights the importance of collaboration between dermatology and genetics clinics."

As reported July 9th online in JAMA Dermatology, Everett of the University of Michigan, Ann Arbor and colleagues reviewed data on 86 patients with SN.

Of these, 25 (29%) had germline MMR mutations confirming Lynch syndrome. Of the 77 patients with immunohistochemical screening of sebaceous neoplasms, 38 (49%) had loss of staining of one or more MMR proteins and 14 had germline MMR mutations.

Immunohistochemical analysis correctly identified 13 of 16 MMR mutation carriers, giving a sensitivity of 81%.

Ten of 12 patients with more than one sebaceous neoplasm had MMR mutations. However, 52% of MMR mutation carriers did not meet clinical diagnostic criteria for Lynch syndrome, and 11 of 25 (44%) did not meet the clinical definition of the Muir-Torre variant of Lynch syndrome.

Therefore, the investigators warn, abnormal immunohistochemical results are not diagnostic of Lynch syndrome and should be interpreted cautiously in conjunction with family history and germline genetic testing.

Everett said initial screening of the neoplastic tissue costs about $700-$800, and follow-up genetic testing to identify inherited mutations can be in the range of $1,000-$3,000, "depending on how many genes we need to check."

"We need further study to determine the best way to use the initial screening test in a cost effective way," she said. "It makes sense to suggest screening a sub-set based on young age or family history criteria, but that will require consistency and standardization in how clinics collect and use family history."

Commenting by email, Dr. Meera Mahalingam of Boston University told Reuters Health that "the current study underscores the utility of immunohistochemistry as a screening tool for Lynch syndrome by reinforcing the sensitivity and ability of this method to detect the involved MMR protein, reproducibility of results using this methodology and, demonstrating a good correlation between results using this method and microsatellite analyses."

Dr. Mahalingam, who has conducted extensive research in this field, added, "On a cautionary note, it is however important to bear in mind that maintenance of expression of the MMR proteins does not exclude the possibility of an underlying DNA repair defect."

SOURCE: http://bit.ly/1js0hsv

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