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Immunohistochemistry in Lymph Node Histiocytosis

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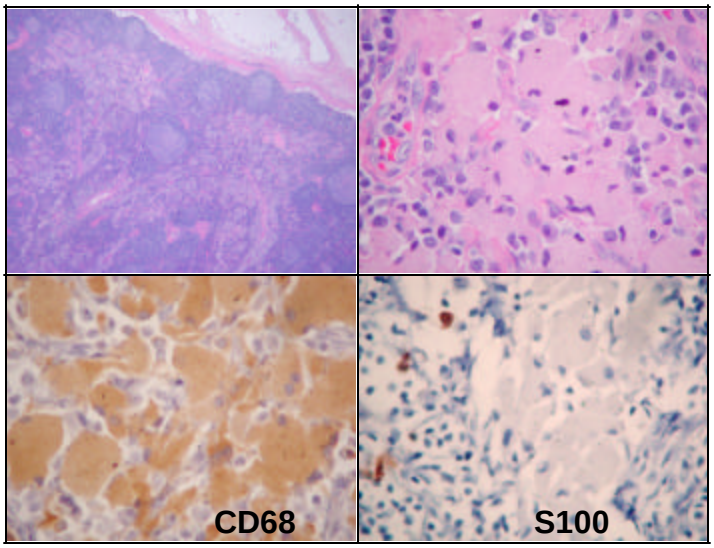
From time to time, diagnostic pathologists encounter lymph nodes that contain a prominent population of histiocytes. Having had a number of such cases referred to our laboratory for immunostaining purposes, I thought it might be of interest to readers to briefly review the common differential diagnostic possibilities to keep in mind, and to discuss the utility of a small panel of immunostains in addressing these cases.

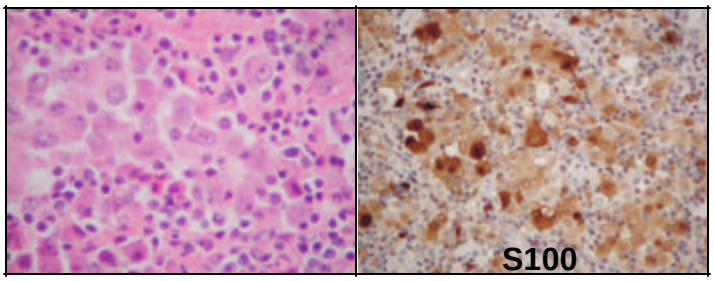
Reactive sinus histiocytosis of lymph nodes is a very common finding , and undoubtedly in many cases it is largely ignored, since it is often of little or no clinical importance. However, when this finding becomes prominent, it can result in a somewhat alarming appearance. The extreme end of this spectrum occurs in cases of reactive histiocytosis related to prior joint replacement surgery, which can closely simulate metastatic carcinoma in some cases. As its name implies, the proliferating histiocytes occur within the lymph node sinuses, and they characteristically express CD68 , but lack S100 protein and CD1a. One typically finds a minority of histiocytes in the background that express S100 protein and CD1a, but the large majority of histiocytes in reactive histiocytosis do not express these markers.



H&E sections (top row) of inguinal lymph node with histiocytosis related to a previous hip replacement. The histiocytes stain nicely with CD68, but are negative for S100 protein. CD1a was also negative.

When **Langerhans cell histiocytosis** involves a lymph node, the proliferating cells occur within the sinuses of the lymph node. The characteristic twisted and convoluted nuclei of Langerhans cell histiocytosis are well described, and in addition to expression of the histiocyte-related marker CD68, they also express S100 protein and CD1a.

Rosai-Dorfman disease (also known as sinus histiocytosis with massive lymphadenopathy, or **SHML**) also demonstrates a prominent proliferation of histiocytes within lymph node sinuses, although they do not

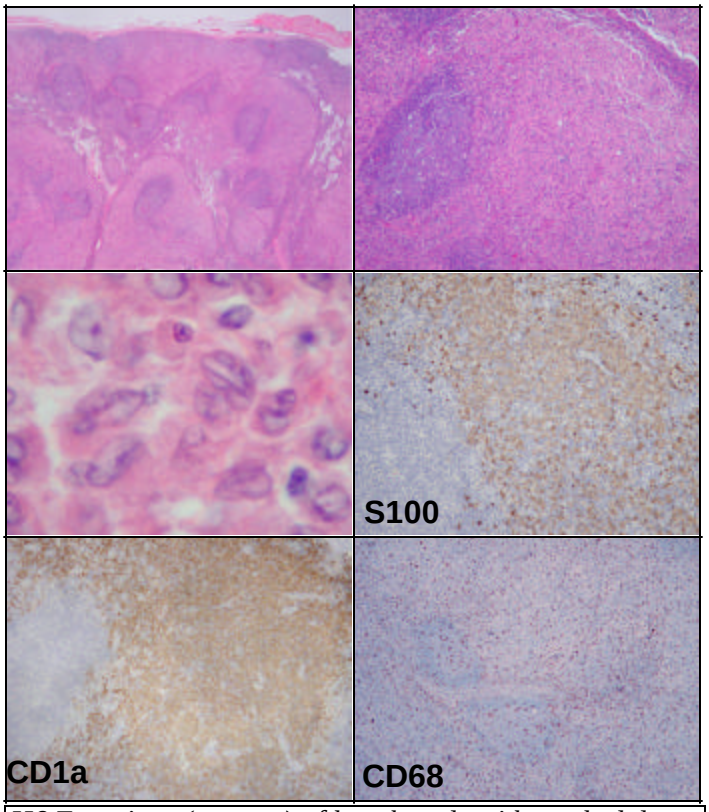


H&E (left) and S100 immunostain (right) on a case of SHML. The histiocytes were also positive with CD68 but were negative with CD1a.

show the nuclear irregularities that are typical of Langerhans cells. Although phagocytosis of lymphocytes by histiocytes in SHML is illustrated in many textbooks and papers, in my own personal experience I have not found it to be as widespread as one would expect from reading the literature. In addition to the histiocyte-related marker CD68, histiocytes in SHML express S100 protein. However, unlike Langerhans cell histiocytosis, they do not express CD1a.

Cases of florid **dermatopathic lymphadenitis** can be alarming at first glance, secondary to large numbers of histiocytes which replace significant areas of the lymph node. Since the proliferating histiocytes in dermatopathic lymphadenitis include a major component of Langerhans cells, twisted and convoluted nuclei are readily appreciated. However, unlike Langerhans cell histiocytosis, the histiocytes in dermatopathic lymphadenitis proliferate in the paracortex rather than the sinuses. To my knowledge dermatopathic lymphadenitis has not been particularly well studied using immunostains, although in several cases that I have seen, it is interesting that the histiocytes have been negative for CD68. As one would expect for Langerhans cells, they express CD1a and S100 protein.

By knowing the immunophenotype and the expected location of proliferating histiocytes in the various entities discussed above, one can usually provide a definitive diagnosis in these cases. Parenthetically, one must also keep in mind that melanomas and some carcinomas express S100 protein and CD68, so if those possibilities are in the differential diagnosis, additional immunostains (cytokeratin, MART-1, etc.) will be needed.



H&E sections (top row) of lymph node with marked dermatopathic lymphadenitis. Note prominent collections of pale histiocytes in the paracortex, that have irregular nuclei when examined under oil (middle row left). The remaining phorographs represent the immunostains when viewed under medium power (10x objective). Note the sheets of histiocytes express S100 and CD1a, but lack CD68 (this has been the phenotype observed in several such cases studied at ProPath). In contrast, cases of Langerhans cell histiocytosis involve the sinuses of the lymph node, and express CD68 as well as S100 and CD1a.

	Location of Histiocytes	CD68	S100	CD1a
Reactive Histiocytosis	Sinuses	POS	Neg	Neg
Langerhans Histiocytosis	Sinuses	POS	POS	POS
SHML	Sinuses	POS	POS	Neg
Dermatopathic Lymphadenitis	Paracortex	Neg *	POS	POS

* Personal Observation - small number of cases

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