primary tumor was in the form of peritoneal thickening in the right upper quadrant, as detected by CT scan.

We have now obtained follow-up information on this patient, courtesy of Dr. Howard C. Adelman, Passaic, NJ, U.S.A. A laparotomy was performed in April 1991. The main operative findings were ascites and multiple peritoneal nodules. Sections from greater omentum and umbilical ligament showed infiltration by a tumor with the typical morphologic and immunohistochemical features of malignant mesothelioma; this tumor was identical to the one seen in the previous lymph node biopsy. Furthermore, cytologic examination of pleural fluid revealed malignant cells consistent with malignant mesothelioma.

Since the case in question was the only one in which the involved lymph node was in the mediastinum, and in view of a recent report proposing the existence of "inclusions" of benign mesothelial cells in this very location (1), we thought it was important to document the fact that our case did indeed represent a metastatic mesothelioma, like all the others in our series.

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Juvenile Xanthogranuloma

To the Editor:

Janney et al. (7) classify juvenile xanthogranuloma as a tumor of "macrophagic-myofibroblastic differentiation." It is difficult to accept this conclusion because differentiation is a process that implies a definition of the original stem cell. What is the stem cell for this tumor? a hematopoietic stem cell or a "vessel wall derived undifferentiated mesenchymal cell" (5)?

The monoclonal antibody HAM-56, which was used by the Janney et al. (7), is not specific for the macrophage because it cross-reacts with smooth muscle cells in human atherosclerosis (3). In addition, according to all appearances, it has also cross-reacted with myofibroblasts in juvenile xanthogranulomas (7). At the same time, monocyte-macrophage–specific antibody MAC-387 has proved negative (7). It should also be stressed that it is difficult to define the macrophage according to morphology (8) because other cell phenotypes, such as the undifferentiated endothelial cell (1,9) or the immature vascular smooth muscle cell (6), may acquire its character and function (2). There is no conclusive evidence, therefore, that a majority of the cells in juvenile xanthogranuloma are macrophages.

At one time, this tumor was known as "naevo-xantho-endothelioma" (10) because a proliferation of vascular endothelial cells was considered to be its main pathogenetic feature. Indeed, the large clear round cells (Fig. 1. in ref. 11) surrounded by a "basement membrane" as defined by light microscopy (Figs. 6., 8. in ref. 12) cannot be macrophages, because macrophages do not secrete collagen into the extracellular space. Instead, they may be identified as undifferentiated vascular endothelial cells phagocytizing lipids and differentiating into myofibroblasts (4).

The name "naevo-xantho-endothelioma" ultimately fell into disrepute. It was replaced by "juvenile xanthogranuloma" (7) because the lesion's tumoral cells were no longer considered to be of endothelial origin but instead were identified as macrophages. This misinterpretation of the vascular endothelial cell in juvenile xanthoma and undoubtly also in other pathological lesions (3) eventually led to an abandonment of the concept of a reticulo-endothelial system and to its replacement by the mononuclear-phagocytic system (5). Lipton et al. (9) have only recently shown that vascular endothelial cells may acquire the properties usually attributed to this system by a process called transdifferentiation. Their contribution should initiate the process of a successive rehabilitation of the old reticulo-endothelial system.

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The Authors' Reply

To the Editor:

We thank Dr. Beranek for his comments. However, the main purpose of our paper (1) was to address the issue of identification of the superficial and deep forms of juvenile xanthogranuloma in a diagnostic context. As surgical pathologists, we use the term "differentiation" to refer to our ability to separate one morphologic process from another in order to render a diagnosis. The concept of "stem cell' is not a useful primary tool in a diagnostic context. A histologic diagnosis is based on a standard that is defined in terms of histosimilarity of a lesion to known concepts of normal tissues or previously defined normal or abnormal cellular processes, such as inflammatory reactions or tumors.

Dr. Beranek's comments are directed more at theoretical, derivative concepts, which are currently unproven. The accumulated evidence regarding juvenile xanthogranuloma suggests that it falls within the spectrum of lesions known as "non-X histiocytoses" (non-Langerhans' cell). To the best of our knowledge, there is no evidence that juvenile xanthogranuloma is a lesion of endothelial cells. Nor is it known where the cells of any particular lesion of juvenile xanthogranuloma originate. So far as we know, the physiological kinetics of the cells in individual lesions has not been addressed in any scientific manner.

Regardless of this apparent dilemma, one fact remains certain: The concept of juvenile xanthogranuloma (i.e., the spectrum of entities represented by that name) remains a useful diagnostic tool for pathologists and clinicians. In addition, it is easily recognized in the context of cutaneous lesions. To learn more about the nature of juvenile xanthogranuloma, one must start by observing lesions within the conceptual spectrum and scientifically testing them for their phenotypic and physiological attributes.

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