The Potential Histogenic Relationship of the Peripheral Nerve to Synovioma

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Abstract

The belief that synoviomas differentiate from the synovial membrane has been widely accepted. Absolute proof is lacking, mainly because precancerous synovial atypia has not been documented in human tissue. During the last 50 years, pain has emerged as one of the significant features of synovioma, occurring very early in the course of the disease in some patients. Gross relationship to nerve, cumulative histological data, and theoretical relationships with three other cancers of neural origin suggest the nerve sheath as an alternate parent tissue for synovioma. Three cases illustrating nerve involvement are included.

Introduction: Problems in Analysis

The histogenesis of synovial sarcoma from synovium has been widely accepted, although exact documentation seems just beyond reach. One of the significant problems in histogenetic studies of this cancer is the fact that a variety of soft tissues constitutes the tumor bed. This spectrum is much less advantageous for determining the cells of origin than is a monomorphic background such as cartilage or notochord. In this situation, origin from undifferentiated mesenchyme with synovioblastic potential is a reasonable possibility (17). Another significant problem in histogenesis is the fact that all human tumors, to our knowledge, have been relatively large when first diagnosed. Large size alone tends to obliterate histogenetic clues such as precancerous atypia and contiguous in situ changes. In this regard, our report of a minute synovioma detected because of tenderness in the absence of a palpable mass in a 34-year-old male is of interest (13). The tumor approximated 4.3 cm and contained nonmyelinated nerves. This finding, together with pertinent data collected by others, suggests that the relationship between nerve tissue and synovioma should be further explored.

Nerves and Pain in Synoviomas of Various Sizes

The detection of nonmyelinated nerves within this synovioma (13) was facilitated by the small volume of the tumor and has not to our knowledge been reported previously. The presence of these nerves offers a reasonable explanation for the prolonged tenderness experienced by this patient and also voices the more controversial possibility that nerves play some role in the induction phase of synovioma or that nerves or perineural mesenchyme may be the parent tissue of synoviomas. Some support for this hypothesis was provided by the report of Pack and Ariel (18) on a group of 11 patients with synovioma who presented with pain or tenderness prior to the appearance of tumor or swelling. The microscopic synovioma that we have reported (13) was capable of producing tenderness almost from its inception. Symptoms occurring prior to the emergence of a palpable tumor, referred to for convenience as the predumor stage, have been amply confirmed by DeSanto et al. (7), Lohr (15), Coley and Pierson (6), Haagensen and Stout (11), Cadman et al. (5), and Thompson et al. (21). This nonpalpable phase may well hold the key to further assessment of the histogenesis of synovioma, since it is in the earlier stages of development that a tumor is most likely to retain identifiable parent tissue showing in situ atypica. Synoviomas have been found in gross continuity with: the brachial plexus [Lohr (15); Batsakis (2); and Pack, Case 17 (18)]; the perineal nerve [DeSanto, Case 15 (7)]; the internal popliteal nerve [Haagensen, Case 1 (11)]; the radial nerve [Haagensen, Case 2 (11)]; and probably the peroneal nerve [Coley, Case 4 (6)].

Apparent Histological Similarity between Synoviomas and Nerve Tumors

Zippel noted myxomatous changes in synoviomas of his patients, Patients 1 and 2 (23). The histochemical nature of mucin found in synoviomas is accounted for by Roth et al. (19). They found hyaluronidase-sensitive mucoid material in stroma outside the pseudoglandular spaces in their group of neck synoviomas. Identical conclusions were reached in a recent study of cutaneous metastases of synovial sarcoma (1). Myxomatous changes were present in the peripheral part of the microscopic tumor in continuity with small nerves. This change is also commonly found in solitary neurofibromas, and the suggestion that interstitial mucin is neural in origin or is reflecting limited neural differentiation within the synovioma comes to mind. When histogenetic considerations are further extended, the role of endoneurium in the formation of nerve sheath myxoma may be important with reference to intercellular secretion as well as to embryological relationships to the meninges. The presence of psammoma bodies in the latter and in meningiomas is a familiar finding. Their concentric nature is strikingly similar to that of the calcipospherites found in about 40% of synoviomas.

A further line of support for some relationship of nerve tissue to synovioma comes from 3 rare tumors which themselves have not been clearly defined: clear cell sarcomas of tendon sheath and aponeuroses; medullopitheliomas of peripheral nerve; and neuroid tumors of infancy. Regardless of their somewhat uncertain status, they retain what is believed to be a valid thread of continuity for histogenetic considerations. The clear cell sarcoma of tendon sheath and aponeuroses is a cancer of the extremities recognized and documented by Enzinger (9). He considered the cancer as a possible variant of synovioma.

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Recently, melanin granules have been found in the tumor and confirmed by ultrastructural analysis by 3 different workers (3, 12, 16), constituting a critical histogenetic clue. If the assumption that clear cell sarcoma is really a variant of synovioma stands the test of time, then it follows that the relationship of synovioma to the neural crest is quite intimate. Somewhat related are the occasional neural crest cancer which has a sarcomatous cartilage component (22) and the fact that the neural crest normally gives rise to mesenchymal structures (4), both being presumptive correlates to the nonepithelial component of synovioma. Melulloepitheliomas are controversial for another reason. They have an acceptable biphasic pattern and can have rather well-developed high columnar secretory epithelium quite closely resembling the well-differentiated synovioma. Their rarity, the resultant lack of tissue available for analysis by modern tissue technique, and the lack of familiarity with their morphological features provide some reason for making melulloepithelioma difficult to accept as an entity. The lesion reported by Lanford and Cohn (14), a large tumor mass (6.25 cm), was contiguous with the medial nerve, recurred to 2 x 2 cm in 4 months, and recurred a second time to 11 x 8 cm about 6 months after the first operation. The recurrence pattern has a similarity to the natural history of many synovias. Its histology is clearly biphasic (Fig. 1A). The epithelioid and glandular schwannomas may also have similar relation to synovias. Also, the unusual neuroid congenital cutaneous tumor reported by DeMoragas and Sarro (8) was characterized by multiple polyoid pigmented cutaneous lesions which lost their pigment, became ulcerated, and finally resulted in the death of the infant at 8 months by tumor hemorrhage. The tumor contained a remarkable histological melange of neoplastic types, including melanoma, synovioma, neuroid structures, and melanotic progonoma. In this light, the occasional synovioma reported as having a pattern simulating rosettes of neurogenous origin (20) may constitute further supportive evidence (Fig. 1B).

Illustrative Cases

Case 1. The patient was a 34-year-old male who had severe localized tenderness for 18 months in the right upper thigh. No palpable mass, signs of inflammation, or history of previous trauma was found. A neurosurgeon suggested that the lateral femoral cutaneous nerve be “released.” A second neurosurgeon used local anesthetics to give temporary relief. When the possibility of a glomus tumor was entertained, the area was excised; preserving the capsule. The tumor did not invade the peripheral nerve relationship (e.g., high frequency of pain, occasional nerve involvement, and the fact that the presence of the latter does not necessarily prove that the nerves gave rise to the tumor. In fact, no one feature favoring nerve relationship (e.g., high frequency of pain, occasional neurotomy character, calcospherites resembling psammoma bodies, and the relation of the tumor to clear cell sarcoma, peripheral nerve medulloepithelioma, and neuroid tumors of infancy) can be considered definitive. Nevertheless, when these isolated facts are viewed together, they seem to give credence sufficient enough to further explore the proposition that synovioma may be neural in origin.
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References


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