50 Years Ago in CORR

Synovial Sarcoma

Kirk J. Anderson, MD and Orliiss Wildermuth, MD CORR 1961;29:55–70

Tracing the history of synovial sarcoma, as with most malignant tumors, is difficult: concepts, terminology, diagnostic tools, and diagnostic criteria have changed with time. These changes have made it difficult to know whether alterations in treatment over time have resulted in lower rates of recurrence and higher rates of survival. The problem is compounded by the relative rarity of some musculoskeletal tumors and the associated need to include collections of cases over long periods of time to have sufficient numbers to meaningfully analyze. The earliest described cases of “synovial sarcoma” likely arise from the late 1800s, although according to Jones and Whitman [4], Simon in 1865 described a case of sarcoma arising from the inner side of the knee and described it as “a hypertrophied sarcomatous synovial fringe.” It is not clear, however, if this tumor arose from the synovial lining. v. Ruediger Rydygier described 10 cases of “primary sarcomas of the knee joint capsule,” nine of which were reported from 1886 until 1904 [13]. From the descriptions, not all of these cases would qualify as synovial sarcomas as we consider them today. Some were localized, stalked lesions that did not recur despite histologic descriptions of sarcoma. Turner, in 1894, described a case of “Primary Sarcoma of the Synovial Membrane” [11], and according to v. Ruediger

Rydygier, Lockwood described another case of “Sarcoma of the Synovial Membrane,” in 1902. Thus, the notion that sarcomas (regardless of the type) could arise from the synovial membrane seems to have been established by the early 1900s. Coley, in his article from 1907 [2], detailed 71 cases of sarcoma of the long bones, not one of which he considered arising from the joint, and along with v. Ruediger Rydygier noted the rare nature of these tumors.

Jones and Whitman, in 1914, perhaps first used the term “synovial sarcoma,” presuming these tumors arose from a synovial membrane [4]. In reviewing all the reported cases they could find (including those mentioned above), they suggested only 17 were “authentic cases of primary synovial sarcoma,” to which they added one. Whether their case was truly what we now consider a synovial sarcoma is suspect because there were two primary cell types: “In this case we have a tumor containing two types of giant-cells, one type being a true tumor cell, and important as indicating rapid and incomplete division of the cells, hence high malignancy. The tumor is a true giant-cell sarcoma.” Today, however, we consider the tumor has two cell types that differ from those described earlier: fibrous or spindle-shaped and epithelial, with most tumors being containing both cell types (biphasic). Haagensen and Stout, in 1944 [3],

recognized the problem of the effect of diagnostic criteria on treatment outcomes: “One might expect that a clear conception of the pathology, degree of malignancy, clinical course and results of treatment could be gained by a perusal of these papers. It is distressing to find that this is not so, chiefly because a very considerable number of cases have been reported as synovial sarcomas which were not such, but, in reality, xanthomatous giant cell tumors, tumor-like hyperplasias of the synovial tissues or other benign lesions curable by simple excision. Thus, the apparent cure rate has been made higher than is in fact the truth.” They described tumors with currently accepted cell types, and in a review of the literature and their own cases, they found 104 cases; they noted, “only three are known to be free from evidence of persistence or metastasis more than five years after treatment.” This is in contrast to a statement by v. Ruediger Rydygier [13], “The prognosis I would say is not too sad, given the slow progression of this disease and the lack of glandular swellings. If in some cases, local recurrences have been observed, for the selected surgical procedure (circumscribed excisions) is to blame.” Perhaps presciently, Haagensen and Stout believed the tissue of mesothelial origin by culturing tissue from three cases and analyzing the cells. They also challenged the notion that the tumors arose from the synovial lining:

50 Years Ago in CORR

“...it is very questionable whether or not they are derived from the normal lining cells of joints, tendon sheaths, and bursae, because the tumors are usually outside of these structures although often in close proximity to them.”

Anderson and Wildermuth published their review in 1961 in CORR® [1]; they reported 27 patients and used histologic criteria similar to that described by Haagensen and Stout. As with past investigators, they noted the tumor occurred primarily in younger adults (average age, 30 years). They emphasized the malignant nature of the tumor but reported a somewhat better prognosis than did the latter authors: at an average followup of nearly 6 years, 13 patients were alive without “active” disease, 13 had died, and one was alive with metastases (Table 1). That said, 21 of the 27 patients had experienced recurrences, all of which were treated either with reexcision or amputation.

Lewis et al. [5] in a series of 122 patients reported in 2000 found 5-year local recurrence, distant recurrence, and mortality rates of 12%, 39%, and 25%, respectively. They noted the following risk factors for higher mortality: tumor size greater than 5 cm and bone or neurovascular invasion. Pitcher [9] suggested a 50% to 80% 5-year overall survival, and noted numerous factors related to worse prognosis: older than 20 years, proximal location, larger than

5 cm, poor differentiation and high mitotic rate, high nuclear grade and aneuploidy, monophasic histology, large percentage of necrosis, vascular invasion, and inability to achieve a wide resection. Evidence during the past two decades suggests synovial sarcoma has a genetic basis [6, 7, 9, 10, 12], related to specific fusion proteins. Naka et al. [8] noted synovial sarcoma was characterized by a unique t(X;18)(p11;q11) chromosomal translocation, and suggested this unique sarcoma may arise from mesenchymal stem cells driven to dysregulation by the SS18-SSX fusion protein. There is little doubt our view of synovial sarcoma will continue to evolve as new methods of observation become available. It remains, however, a deadly tumor to many.

Table 1 Survey Résumé of 27 Cases of Synovial Sarcoma

1. Average age of patients at onset of symptoms: 30 yrs.
2. Sex of patients: male, 16; female, 11
3. Location of tumor
Para-articular, 20; intra-articular, 4; no joint relationship, 3
Joint involved
Metacarpophalangeal, 1; wrist, 5; shoulder, 4; metatarsophalangeal, 1; ankle, 3; knee, 10
Site of tumors without joint relationship
Thigh, 2; forearm, 1

Table 1 continued

4. Average duration period of tumor before treatment: 35 mos.
5. Symptoms
History of trauma: 6 cases
Pain: 14 cases
Swelling: 27 cases
Joint dysfunction: 8 cases
Palpable tenderness of the tumor: 4 cases
6. Roentgenographic appearance
Soft-tissue tumor: 9 cases
Bone erosion: 6 cases
Calcification in tumor: 2 cases
Negative roentgenogram: 18 cases
Calcification in metastatic tumor: 1 case
7. Treatment
Cases treated by local excision only: 10
Cases treated by primary amputation: 9
Cases treated by delayed amputation: 8
8. Incidence of recurrence after excision: 21
9. Metastases
Number of cases with metastatic disease: 15
Location of metastasis: lung, lymph nodes, liver, adrenal gland, bone
10. Follow-up
Average period of follow-up: 5 yrs. 11 mos.
11. Results
Patients alive with no active disease: 13
Patients alive with metastasis: 1
Patients dead: 13

Table 1 from the article Synovial Sarcoma by Anderson and Wildermuth is shown. (Reprinted with permission and © Lippincott Williams & Wilkins from Anderson KJ, Wildermuth O. Synovial sarcoma. *Clin Orthop Relat Res.* 1961;19:55–70.)

50 Years Ago in CORR

Richard A. Brand MD
Editor-in-Chief
*Clinical Orthopaedics
and Related Research*

References

1. Anderson KJ, Wildermuth O. Synovial sarcoma. *Clin Orthop Relat Res*. 1961;19:55–70.
2. Coley WB. Sarcoma of the long bones: the diagnosis, treatment and prognosis, with a report of sixty-nine cases. *Ann Surg*. 1907;45:321–368.
3. Haagensen CD, Stout AP. Synovial sarcoma. *Ann Surg*. 1944;120:826–842.
4. Jones SF, Whitman RC. Primary sarcoma of the lower end of the femur involving the synovial membrane: with a critical review of the literature of synovial sarcoma. Report of one case with complete pathological and radiographic examination. *Ann Surg*. 1914;60:440–450.
5. Lewis JJ, Antonescu CR, Leung DH, Blumberg D, Healey JH, Woodruff JM, Brennan MF. Synovial sarcoma: a multivariate analysis of prognostic factors in 112 patients with primary localized tumors of the extremity. *J Clin Oncol*. 2000;18:2087–2094.
6. Limon J, Mrozek K, Mandahl N, Nedoszytko B, Verhest A, Rys J, Niezabitowski A, Babinska M, Nosek H, Ochalek T, et al. Cytogenetics of synovial sarcoma: presentation of ten new cases and review of the literature. *Genes Chromosomes Cancer*. 1991;3:338–345.
7. Limon J, Mrozek K, Nedoszytko B, Babinska M, Jaskiewicz J, Kopacz A, Zoltowska A, Borowska-Lehman J. Cytogenetic findings in two synovial sarcomas. *Cancer Genet Cytogenet*. 1989;38:215–222.
8. Naka N, Takenaka S, Araki N, Miwa T, Hashimoto N, Yoshioka K, Joyama S, Hamada K, Tsukamoto Y, Tomita Y, Ueda T, Yoshikawa H, Itoh K. Synovial sarcoma is a stem cell malignancy. *Stem Cells*. 2010;28:1119–1131.
9. Pitcher JD Jr. Synovial Sarcoma. 2009. OrthopaedicsOne. Available at: <http://www.orthopaedicsone.com/display/PORT/Synovial+Sarcoma>. Accessed December 27, 2012.
10. Turc-Carel C, Dal Cin P, Limon J, Li F, Sandberg AA. Translocation X;18 in synovial sarcoma. *Cancer Genet Cytogenet*. 1986;23:93.
11. Turner AL. Primary sarcoma of the synovial membrane. *Lancet*. 1894;144:54.
12. Uchida A, Seto M, Hashimoto N, Araki N. Molecular diagnosis and gene therapy in musculoskeletal tumors. *J. Orthop. Sci*. 2000;5:418–423.
13. v Ruediger Rydygier AR. Zur Diagnose und Therapie des primären Sarkoms der Kniegelenkkapsel. *Langenbecks Arch Klin Chir Ver Dtsch Z Chir*. 1907;82:211–225.

50 Years Ago in CORR

Synovial Sarcoma
Kirk J. Anderson, MD and
Orliss Wildermuth, MD

Richard A. Brand MD