General Reviews

Ferner and O’Doherty (15) review recent advances in the understanding of the clinical characteristics and pathogenesis of neurofibromas and schwannomas associated with the neurofibromatoses.

Tucker and Friedman (52) review the pathogenesis of hereditary tumors and exceptions to the “two-hit” hypothesis.

NF1 Reviews

Lynch and Gutmann (31) review NF1.

Tormey (50) reviews milestones in the evolution of pheochromocytoma diagnosis.

NF2 Reviews

Sun et al. (48) review the protein 4.1 tumor suppressors and their role in growth regulation. They propose a model for merlin growth regulation in which CD44 links growth signals from the plasma membrane to the nucleus by interacting with ERM proteins and merlin.

Neurofibromatosis Type 1 (NF1)

NF1 Clinical

Arigon et al. (2) evaluated the usefulness of ophthalmologic examination for diagnosis and detection of complications in adult patients with NF1. They found that the contribution of ophthalmologic examination in diagnosis and to the detection of complications is low and should only be performed in patients for whom questioning and clinical examination fail to give evidence of NF1.

Friedrich et al. (16) examined twenty-two patients with NF1 clinically and radiologically to determine the malformations of the maxillary sinuses. They found that only patients with facial plexiform neurofibromas had malformations of the maxillary sinuses. They provide evidence that in the midfacial region the overgrowth is predominantly caused by the plexiform neurofibroma itself and that the bones can be hypoplastic and show scoliosis-like malformation compared to the nonaffected side.

Joossens et al. (25) describe an unusual case of NF1 diagnosed with MRI and associated with hearing loss. Both the enhancement features and the localization in the cerebellum and corpus callosum are atypical.

Moiton et al. (34) describe the case report of a patient with NF1 and associated primary
hyperparathyroidism. Cinamon et al. (8) describe the case report of a 50-year-old woman with NF1 and a 3-year documented history of untreated hyperparathyroidism and a parathyroid adenoma. The patient also developed a mandibular osteogenic sarcoma. They speculate that untreated hyperparathyroidism in NF1 patients may lead to induction and growth of osteogenic sarcomas.

Cutting et al. (9) studied eighteen male patients with NF1 and found that the increase in frontal and parietal white matter volumes supports the hypothesis that NF1’s white matter pathology encompasses but is not limited to visible UBO. Male patients with NF1 and ADHD, as compared with patients with NF1 alone, showed frontal reductions that are largely consistent with those found in idiopathic ADHD.

Mizuno et al. (33) describe the case report of a 67-year-old woman with a right-sided thoracic meningocele associated with NF1 that had been asymptomatic for 20 years. She presented with dyspnea and MRI imaging revealed progression of a giant meningocele associated with hydrothorax. Laminoplasty with incision of the meningocele and dural plasty was performed successfully.

Ogose et al. (38) describe the case report of a 42-year-old woman with NF1 and an intrathoracic meningocele. Immunohistochemical and cytogenetic findings from the resected tumor strongly suggest that a subset of intrathoracic meningoceles have a tumoral nature rather than simple herniation of the meninges.

Tubbs and Oakes (51) describe the case report of a 15-year-old female with NF1 and associated dural ectasia. The distal meningocele presented as an ovarian cyst.

Becelli et al. (5) describe the case reports of two individuals with NF1 with palatal localization and discuss the diagnostic and surgical problems they encountered. Sanchez and Siuda (45) describe a probable case of NF1.

**NF1 Imaging**

Gupta et al. (18) describe the radiological features of NF1 in a 16-year-old boy with café-au-lait spots. Kassai et al. (26) present the endosonographic appearance of a rectal neurofibroma which showed an hourglass shape.

El-Koussy et al. (13) describe the perfusion MRI abnormalities in the absence of diffusion changes in a case of moyamoya-like syndrome in a 12-year-old boy with NF1.

Halefoglu (19) suggest that MR, especially T2-weighted images with very high signal intensity, is a very useful and sensitive modality in the accurate diagnosis of NF1. Imbert et al. (22) discuss the value of MRI in a case report involving neurofibromatosis of the liver.
NF1 Orthopedic Features

Yang and Lee (58) describe the case reports of three children with isolated congenital pseudoarthrosis of the fibula. Two of the three children had NF1.

NF1 Vascular Features

Dluhy (10) discusses screening for genetic causes of hypertension including hereditary pheochromocytomas associated with NF1.

Dominguez et al. (11) describes the case report of a 44-year-old man with NF1 and acute hemothorax caused by intercostal artery aneurysm rupture. He was successfully treated with percutaneous embolization. Hines et al. (20) describe the case report of a 52-year-old man that suffered an infrarenal aortic rupture secondary to NF1.

Ohta et al. (39) describe the case report of a 22-year-old man with hypoplasia of the internal carotid artery at the cervical portion associated with NF1.

NF1 Tumors

Andrassy (1) reviews the advances in the surgical management of sarcomas in children.

Rabii et al. (42) describe the case report of a 49-year-old woman with pheochromocytoma associated with NF1.

Nakamura et al. (35) describes a case of NF1 associated with a duodenal gastrointestinal stromal tumor and carcinoma of the sigmoid colon.

Magro et al. (32) describe floretlike multinucleated giant cells in a neurofibroma from a patient with NF1.

NF1 Gene and Tumor Biology

Rechitsky et al. (43) presents results of preimplantation genetic diagnosis (PGD) for cancer predisposition syndromes including NF1 and NF2.

Pacheco et al. (40) performed a linkage study in a large family affected with multiple lentigines syndrome (MLS) in order to identify the gene(s) responsible for MLS. The NF1 gene was excluded as the cause of MLS in this family.

Van Roy et al. (55) localized the 17q breakpoint of a constitutional 1;17 translocation in a patient with neuroblastoma within a 25-kb segment located between the ACCN1 and TLK2 genes and near the distal breakpoints of two microdeletions in patients with NF1. They suggest that this chromosomal region is genetically unstable and prone to rearrangements.
Fang et al. (14) genotyped 19 French Canadian families with NF1 in the Quebec population using four intragenic microsatellites. Linkage analysis indicates that the four microsatellites are strongly linked with NF1 disease. No founder effect for NF1 was detected in the Quebec French Canadians.

Kotsuji-Maruyama et al. (28) demonstrated that PDGF-BB induces MAP kinase phosphorylation and VEGF expression in neurofibroma-derived cultured cells from patients with NF1. This stimulation may be important in neurofibroma hypervascularization.

Xu et al. (57) showed that gene-targeted deletion of neurofibromin enhances the expression of a transient outward K+ current in Schwann cells via a protein kinase A-mediated mechanism.

Nakayama and Terao (36) found that various neurofibroma cells lines isolated from either dermal, plexiform, or diffuse neurofibromas respond to human gamma interferon by decreasing proliferation rates in vitro.

Rizvi et al. (44) demonstrate that wounding causes pigmentation of nerve-derived glial cells and that the βc receptor, via Nf1, normally suppresses melanogenesis after injury.

Ingram et al. (23) demonstrated that neurofibromin functions as a critical negative regulator of Ras and T-cell homeostasis in vivo.

Donovan et al. (12) found that the pleiotropic effects of hyperactive Ras in Nf1-deficient cells are mediated through discrete downstream signaling cascades that cooperate to undermine growth control. Aberrant GM-CSF expression is likely to reinforce aberrant growth through an autocrine loop that further deregulates Ras signaling.

Kraemer et al. (29) used fluorescently labeled guanine nucleotide binding proteins to analyze elementary steps of GAP-catalyzed reactions. They showed that three different GAPs (p120-GAP, NF1, and Rap1GAPv) display highly different dynamics of binding and catalysis.

Using heterozygous mice with a mutant allele neogene inserted into exon 31 of Nf1, Kimura et al. (27) hypothesize that the tumorigenesis of composite pheochromocytoma is as follows: The loss or decrease of neurofibromin may induce proliferation of Schwann cells and sustentacular cells and also induce an increase in neurotrophic factors that may cause proliferation of ganglionic cells and pheochromocytoma cells through both autocrine and paracrine loops. Finally, these cells form a composite pheochromocytoma.

Tischler (49) showed that recently described pheochromocytoma cell lines from neurofibromatosis knockout mice are novel models for signaling by the receptor tyrosine kinase ret. They also suggest that purified enterochromaffin-like (ECL) cells may offer new opportunities to study the shared and distinctive aspects of neuroendocrine function using a normal cell type.
Powers et al. (41) determined that adrenergic mouse pheochromocytoma (MPC) cells may have direct relevance to human pheochromocytomas and may be useful for studying the roles of both neurofibromin and Ret in the development of those tumors.

**Neurofibromatosis Type 2 (NF2)**

**NF2 Clinical**

Baser et al. (4) evaluated the clinical diagnostic criteria for NF2. They determined that none of the existing sets of criteria are adequate at initial assessment for diagnosing people who present without bilateral vestibular schwannomas as having NF2, particularly people with a negative family history of NF2. They recommend that a single, revised set of diagnostic criteria be devised to replace the four existing sets of criteria.

Valeviciene (54) describes the case report of a 37-year-old female with NF2.

**NF2 Tumors**

Cihangiroglu et al. (7) describe the case report of a 32-year-old woman with a laryngeal neurofibroma associated with NF2. Laryngeal neurofibromas have previously been reported in cases of NF1, but their presence has not been described in a patient with NF2.

Ho and Kveton (21) describe a rare complication of stereotactic radiotherapy for large acoustic neuromas in a patient with NF2. A 14-year-old girl with NF2 underwent stereotactic radiotherapy for treatment of two acoustic neuromas. Follow-up MRI 7 months following radiotherapy demonstrated a rapid growth of the acoustic neuromas. Their findings suggest that the radiotherapy might have been the cause of the rapid growth of the acoustic neuromas. They argue against the use of radiotherapy as the primary treatment modality for patients with NF2 and acoustic neuromas that are already compressing the brainstem.

Jarmundowicz et al. (24) summarize their experience in the surgical treatment of tumors of the brachial plexus. Two of the five cases discussed involved tumors associated with NF2. Li et al. (30) describe MRI diagnosis of tumors involving the brachial plexus in China. Three of the thirteen patients examined had neurofibromatosis. They found that the coronal position of T1W1 could clearly represent the relationship between brachial plexus and tumor.

**NF2 Gene and Tumor Biology**

Rechitsky et al. (43) presents results of preimplantation genetic diagnosis (PGD) for cancer predisposition syndromes including NF1 and NF2.

Buckley et al. (6) constructed a full-coverage, high-resolution human chromosome 22 genomic microarray for clinical and research applications.
Noguera Julian et al. (37) describe the case of a 12-year-old girl with NF2 as a result of a de novo mutation.

Bannykh et al. (3) describe the case report of a 52-year-old man with a malignant rhabdoid meningioma arising in the setting of a preexisting ganglioglioma. The man was without stigmata of NF2, but FISH revealed loss of one copy of NF2.

Gautreau et al. (17) isolated and characterized an aggresome determinant in the NF2 tumor suppressor.

Scoles et al. (46) showed that both schwannomin and its interacting protein, hepatocyte growth factor-regulated tyrosine kinase substrate (HRS), are inhibitors of STAT activation in human and mouse schwannoma cell lines. They also found that schwannomin with a naturally occurring NF2 missense mutation that alters HRS binding abolishes the ability for schwannomin to inhibit STAT activation.

The results of Sun et al. (47) suggest that merlin growth suppression requires HRS expression and that the binding of merlin to HRS may facilitate its ability to function as a tumor suppressor.

Xiao et al. (56) showed that merlin is phosphorylated in response to expression of activated Rac and activated Cdc42 in mammalian cells. They also demonstrated that merlin phosphorylation is mediated by p21-activated kinase (Pak), a common downstream target of both Rac and Cdc42. Both in vivo and in vitro kinase assays demonstrated that Pak can directly phosphorylate merlin at serine 518, a site that affects merlin activity and localization.

Schwannomatosis

Ture et al. (53) describe the case report of a 31-year-old male with a trochlear nerve schwannoma and no evidence of neurofibromatosis. The tumor was totally resected without additional morbidity using an infratentorial lateral supracerebellar approach.

Reference List


[Neurofibromatosis type 2 as a result of a de novo mutation: a case report].


21):3991-4000.


