NFLAMMATION of the pineal gland is rare. To our knowledge, there have been no prior case studies of a primary inflammatory process restricted to the pineal gland (pinealitis) that was not associated with a pineal tumor or other inflammatory process in the posterior thalamic region. We present the case of a chronic inflammatory process of the pineal gland of unknown origin. The clinical and pathological features of this remarkable case, including radiological, light microscopy, and immunohistochemical studies, are delineated.

Case Report

History. This 63-year-old man sought medical attention because of the onset, 2 or 3 months earlier, of the sensation of falling backward while walking up the stairs. More recently he had begun to notice increasing headaches, nasal congestion, and stuffiness. There was no evidence of impairment of memory, gait difficulties, or sensory or motor deficits. There were no visual disturbances, and he did not have bladder or bowel dysfunction.

Examination. Results of a physical examination including neurological testing were unremarkable. No focal abnormalities were noted, extraocular movements were full, including conjugate, horizontal, and vertical gaze; and an ophthalmological examination revealed no sign of uveitis or other disease. A magnetic resonance (MR) imaging study demonstrated a 1.8 × 1.4 × 1.2-cm mass at the posterior third ventricle just anterior and superior to the superior colliculus. The lesion appeared isointense to brain on the T1-weighted MR images, hyperintense to brain parenchyma on the spin-density images, and slightly heterogeneous on the T2-weighted images. It enhanced with administration of gadolinium. The mass caused obstructive hydrocephalus with marked dilation of the third and lateral ventricles, and there was transependymal migration of cerebrospinal fluid (CSF). There was a small lacunar...
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infarct in the left pons, but no other enhancing lesions were observed throughout the brain parenchyma (Fig. 1).

Operation. The patient underwent an occipital craniotomy while in the lateral decubitus position. We used a suboccipital transtentorial approach; an abnormal mass was found in the pineal region below the internal cerebral veins. It was quite circumscribed and separable from the thalamus and the brainstem; it was totally removed without injuring the colliculi or any neighboring vessels.

Postoperative Course. The patient’s recovery was uneventful, and he was discharged on the 6th postoperative day. He continues to be somewhat confused 18 months after his operation.

Pathological Findings. Multiple irregular fragments of soft tissue that was tannish brown and firm were submitted for pathological evaluation (Fig. 2). Hematoxylin and eosin–stained sections of paraffin-embedded blocks showed that the tissue consisted of pineal parenchymal cells aggregated in lobules delimited by glial tissue. The lobules were surrounded and infiltrated by inflammatory cells consisting of admixtures of eosinophils, lymphocytes, plasma cells, macrophages, and scattered mast cells. Scattered multinucleated cells associated with calcified, nonpolarizable material were present. No epithelioid histiocytes, granulomas, or foci of necrosis were identified. Immunohistochemical analysis was performed using a panel of antibodies (Table 1). The pineal parenchymal cells were strongly positive to synaptophysin staining and could be definitively identified using silver impregnation and SMI-31 (a neurofilament protein marker); glial fibrillary acidic protein–positive astrocytes surrounded the pineal lobules and were found scattered within them. Inflammatory cells consisted of a predominance of eosinophils (Giemsa), and scattered T (CD3) and B (CD20) lymphocytes, mast cells (mast cell tryptase), and rare macrophages (CD68). The lymphoid population consisted mainly of small lymphocytes that lacked cytological atypia. There was no evidence of Langerhans cells (S-100 and CD1a); other markers were negative: germ cells (placental alkaline phosphatase [PLAP]), neuroendocrine cells (chromogranin), pankeratin, and epithelial membrane antigen. Results of staining for microorganisms were negative for fungi (periodic acid–Schiff and methenamine silver stain), and bacteria (Gram’s stain). No viral inclusions or parasites were seen in multiple levels examined. Results of immunoperoxidase studies for toxoplasma were negative.

Discussion

The surgical management of mass lesions in the region of the pineal gland has been controversial.

Chronic inflammatory cells (primarily T lymphocytes) have been described in the pineal region in germ cell tumors and in other neoplasms, including gliomas. Lymphocyte infiltration along fibrovascular septae is a usual feature of germinomas, in which the granulomatous...
element may be the dominant component but with a lower frequency than gonadal germomas. However, careful search for tumor cells and the application of a broad panel of immunohistochemical stains to the section failed to reveal any evidence of neoplasia in this case. Because it has been long recognized that the inflammatory process in germ cell tumors can be remarkably localized to a portion of the lesion, it would be possible to sample exclusively the portion of the tumor that shows inflammation. However, in our case the entire pineal gland was excised and the tissue was subjected to multiple sections, thereby excluding the possibility of a germ cell tumor. Furthermore, the composition of the inflammatory cells in our case, with a preponderance of eosinophils and a lack of discrete granulomas, is not altogether in keeping with the inflammatory response observed in germ cell tumors.

There was also no evidence of a lymphoproliferative process or of a histiocytosis; all markers for Langerhans’ cells were negative. Populations of T and B lymphocytes were distributed throughout the process and lacked the cellularity, monomorphism, and cytological atypia characteristic of lymphomatous involvement. We interpreted this lesion as possibly related to an autoimmune process, and in attempting to understand it we drew from several embryological and experimental studies.

The pineocyte is a cell with photosensory and neuroendocrine functions; the ontogeny of the human pineal gland recapitulates the phylogeny of the retina and pineal organ. During late stages of intrauterine life and the early postnatal period, the human pineal gland consists primarily of cells arranged in rosettes similar to those of the developing retina. A decrease in nocturnal peaks of the pineal neurohormone melatonin has been observed in patients...
with uveitis, as has radiological evidence of pineal gland disease. There is as yet no direct evidence of pineal gland disease coincident with naturally occurring uveitis, because specimens of pineal gland are not available during an active uveitis. Pinealitis accompanying equine recurrent uveitis was studied in a horse that became blind during an episode of postleptospiral equine recurrent uveitis. The pineal gland in this horse exhibited significant inflammatory infiltration consisting mainly of lymphocytes with some eosinophils. Lymphocytic infiltration of the pineal gland has also been reported in otherwise normal horses, rodents, and in humans. The experimental studies of Kalsow and Wacker have shown that an immune-mediated chronic inflammation of the pineal gland can be produced by sensitization with photoreceptor cell–specific autoantigens. An autoimmune response in both the eye and the pineal gland is not unexpected because both retinal photoreceptor cells and pinealocytes contain the photoreceptor cell–specific proteins used for sensitization: that is, S-antigen, interphotoreceptor cell retinoid binding protein, or rhodopsin. There was no evidence of uveitis in our patient, either preoperatively or during the postoperative follow up. Moreover, melatonin was not measured.

Conclusions

Chronic pinealitis is a distinctive, previously unrecognized, inflammatory lesion of the pineal gland of unknown origin. This entity may be added to the classification of pineal mass lesions of neurosurgical importance.

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